



STIC Search Report

Biotech-Chem Library

STIC Database Tracking Number: 123596

TO: Maury Audet
Location: REM/3D20/3D11
Art Unit: 1654
Thursday, June 03, 2004

Case Serial Number: 09/937484

From: Barb O'Bryen
Location: Biotech-Chem Library
Remsen 1A69
Phone: 571-272-2518 *BOB*

barbara.obryen@uspto.gov

Search Notes

RUSH

Maury,

ECL is also an acronym of for enterochromaffin-like (cells). This lead to false drops. Neither ECL or ECA produced useful hits, so they don't appear in the queries I've printed.

Barb

From: Chan, Christina
Sent: Wednesday, June 02, 2004 4:18 PM
To: Audet, Maury; STIC-Biotech/ChemLib
Subject: RE: 09/937484-RUSH Conjugate/Compound Search

Please rush. Thanks Chris

Chris Chan

TC 1600 New Hire Training Coordinator and SPE 1644 & 1642
(571)-272-0841
Remsen, 3E89

-----Original Message-----

From: Audet, Maury
Sent: Wednesday, June 02, 2004 1:23 PM
To: STIC-Biotech/ChemLib; Chan, Christina
Subject: 09/937484-RUSH Conjugate/Compound Search

Greetings,

If possible could I please get a RUSH search (2 month amended) on the following:

Registry/CAPLus, etc. search of (method of use):

TREATMENT of C-FIBRE NEURON ACTIVITY USING:

Compound alone of "Erythrina cristagalli lectin" or ECL or ECA (referred to by all three names/abbrev.)

OR

The same compound within any type of conjugate/composition.

This is the elected invention, no other species (however, if nothing is found, a search for LECTINS generally for treatment of C-fibre NEURON activity or ANY NEURON activity could be done; sorry I don't have more - this is a pretty indefinite treatment possibility Applicant's have claimed).

I do not have the structure attached (but hopefully it comes up alright by name in a Registry/STN search of compound), but the lectin is a glycopeptide/protein isolated from such sources as castor beans and coral trees (I believe the latter as well).

I have term searched for some time for the use of this compound in such a method, but have not found a lot, so wanted to follow up with your expertise.

Thanks, Maury

Maury Audet
Patent Examiner A.U. 1654
REM 3D20
Mail Box REM 3D11

Searcher: _____
Phone: _____
Location: _____
Date Picked Up: _____
Date Completed: _____
Searcher Prep/Review: _____
Clerical: _____
Online time: _____

TYPE OF SEARCH:
NA Sequences: _____
AA Sequences: _____
Structures: _____
Bibliographic: _____
Litigation: _____
Full text: _____
Patent Family: _____
Other: _____

VENDOR/COST (where applic.)
STN: _____
DIALOG: _____
Questel/Orbit: _____
DRLink: _____
Lexis/Nexis: _____
Sequence Sys.: _____
WWW/Internet: _____
Other (specify): _____



STIC SEARCH RESULTS FEEDBACK FORM

Biotech-Chem Library

Questions about the scope or the results of the search? Contact *the searcher or contact*:

Mary Hale, Information Branch Supervisor
Remsen Bldg. 01 D86
571-272-2507

Voluntary Results Feedback Form

➤ I am an examiner in Workgroup: Example: 1610

➤ Relevant prior art **found**, search results used as follows:

- ☐ 102 rejection
- ☐ 103 rejection
- ☐ Cited as being of interest.
- ☐ Helped examiner better understand the invention.
- ☐ Helped examiner better understand the state of the art in their technology.

Types of relevant prior art found:

- ☐ Foreign Patent(s)
- ☐ Non-Patent Literature
(journal articles, conference proceedings, new product announcements etc.)

➤ Relevant prior art **not found**:

- ☐ Results verified the lack of relevant prior art (helped determine patentability).
- ☐ Results were not useful in determining patentability or understanding the invention.

Comments:

Drop off or send completed forms to STIC-Biotech-Chem Library Remsen Bldg.



=> fil capl; d que l6; fil medl; d que l34; fil embase; d que l49
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FILE COVERS 1907 - 3 Jun 2004 VOL 140 ISS 23
FILE LAST UPDATED: 2 Jun 2004 (20040602/ED)

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'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

inventors

L1 499 SEA FILE=CAPLUS ABB=ON FOSTER K?/AU
L2 31 SEA FILE=CAPLUS ABB=ON CHADDOCK J?/AU
L3 9 SEA FILE=CAPLUS ABB=ON L1 AND L2
L4 351 SEA FILE=CAPLUS ABB=ON QUINN C?/AU
L5 8 SEA FILE=CAPLUS ABB=ON L3 AND L4
L6 1 SEA FILE=CAPLUS ABB=ON FIBER/TI AND L5

FILE 'MEDLINE' ENTERED AT 12:55:55 ON 03 JUN 2004

FILE LAST UPDATED: 2 JUN 2004 (20040602/UP). FILE COVERS 1951 TO DATE.

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MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

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L23 369 SEA FILE=MEDLINE ABB=ON FOSTER K?/AU
L24 14 SEA FILE=MEDLINE ABB=ON CHADDOCK J?/AU
L25 277 SEA FILE=MEDLINE ABB=ON QUINN C?/AU
L27 34004 SEA FILE=MEDLINE ABB=ON PLANT LECTINS+NT/CT
L28 61554 SEA FILE=MEDLINE ABB=ON LECTINS+NT/CT
L29 152 SEA FILE=MEDLINE ABB=ON ERYTHRINA/CT
L34 2 SEA FILE=MEDLINE ABB=ON L23 AND L24 AND L25 AND (L27 OR (L28 AND L29))

FILE 'EMBASE' ENTERED AT 12:55:55 ON 03 JUN 2004
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FILE COVERS 1974 TO 28 May 2004 (20040528/ED)

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L40 300 SEA FILE=EMBASE ABB=ON FOSTER K?/AU
L41 11 SEA FILE=EMBASE ABB=ON CHADDOCK J?/AU
L42 213 SEA FILE=EMBASE ABB=ON QUINN C?/AU
L44 330 SEA FILE=EMBASE ABB=ON ERYTHRINA
L49 1 SEA FILE=EMBASE ABB=ON (L40 OR L41 OR L42) AND L44

=> dup rem l34,l6,l49

FILE 'MEDLINE' ENTERED AT 12:55:56 ON 03 JUN 2004

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PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L6
PROCESSING COMPLETED FOR L49

L82 3 DUP REM L34 L6 L49 (1 DUPLICATE REMOVED)
ANSWERS '1-2' FROM FILE MEDLINE
ANSWER '3' FROM FILE CAPLUS

=> d iall 1-2; d ibib ed ab 3

L82 ANSWER 1 OF 3 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2002470902 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12105193
TITLE: Inhibition of release of neurotransmitters from rat dorsal
root ganglia by a novel conjugate of a Clostridium
botulinum toxin A endopeptidase fragment and Erythrina
crystagalli lectin.
AUTHOR: Duggan, Michael J; Quinn Conrad P; Chaddock
John A; Purkiss John R; Alexander Frances C G; Doward
Sarah; Fooks Sarah J; Friis Lorna M; Hall Yper H J; Kirby
Elizabeth R; Leeds Nicola; Mouldsdaile Hilary J; Dickenson
Anthony; Green G Mark; Rahman Wahida; Suzuki Rie; Shone
Clifford C; Foster Keith A
CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down,
Salisbury, Wiltshire SP4 0JG, United Kingdom.
SOURCE: Journal of biological chemistry, (2002 Sep 20) 277 (38)
34846-52.
Journal code: 2985121R. ISSN: 0021-9258.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020917

Last Updated on STN: 20030105
Entered Medline: 20021024

ABSTRACT:

Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Here we report that a catalytically active derivative (termed LH(N)/A) of the type A neurotoxin from *Clostridium botulinum* has been coupled to a lectin obtained from *Erythrina cristagalli* to form a novel conjugate. This conjugate exhibits an in vitro selectivity for nociceptive afferents compared with the anatomically adjacent spinal neurons, as assessed using in vitro primary neuronal culture systems to measure inhibition of release of neurotransmitters. Chemical conjugates prepared between *E. cristagalli* lectin and either natively sourced LH(N)/A or recombinant LH(N)/A purified from *Escherichia coli* are assessed, and equivalence of the recombinant material are demonstrated. Furthermore, the dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 is demonstrated through the use of an endopeptidase-deficient LH(N)/A conjugate variant. The duration of action of inhibition of neurotransmitter released by the conjugate in vitro is assessed and is comparable with that observed with *Clostridium botulinum* neurotoxin. Finally, in vivo electrophysiology shows that these in vitro actions have biological relevance in that sensory transmission from nociceptive afferents through the spinal cord is significantly attenuated. These data demonstrate that the potent endopeptidase activity of clostridial neurotoxins can be selectively retargeted to cells of interest and that inhibition of release of neurotransmitters from a neuronal population of therapeutic relevance to the treatment of pain can be achieved.

CONTROLLED TERM: Check Tags: Support, Non-U.S. Gov't
Animals
Base Sequence
Botulinum Toxins: CH, chemistry
*Botulinum Toxins: PD, pharmacology
Cells, Cultured
DNA Primers
Endopeptidases: IP, isolation & purification
*Endopeptidases: PD, pharmacology
*Ganglia, Spinal: DE, drug effects
Ganglia, Spinal: ME, metabolism
*Lectins: PD, pharmacology
*Neurotransmitters: ME, metabolism
Peptide Fragments: IP, isolation & purification
*Peptide Fragments: PD, pharmacology
*Plant Lectins
Rats
Recombinant Proteins: CH, chemistry
Recombinant Proteins: IP, isolation & purification
Recombinant Proteins: PD, pharmacology

CHEMICAL NAME: 0 (Botulinum Toxins); 0 (DNA Primers); 0 (Lectins); 0 (Neurotransmitters); 0 (Peptide Fragments); 0 (Plant Lectins); 0 (Recombinant Proteins); 0 (erythrina lectin); EC 3.4.- (Endopeptidases)

L82 ANSWER 2 OF 3

ACCESSION NUMBER: 2000231793 MEDLINE

DOCUMENT NUMBER: PubMed ID: 10768948

TITLE: Inhibition of vesicular secretion in both neuronal and nonneuronal cells by a retargeted endopeptidase derivative of *Clostridium botulinum* neurotoxin type A.

AUTHOR: Chaddock J A; Purkiss J R; Friis L M; Broadbridge J D; Duggan M J; Fooks S J; Shone C C; Quinn C P; Foster K A

CORPORATE SOURCE: Centre for Applied Microbiology & Research, Porton Down, Salisbury, Wiltshire SP4 0JG, United Kingdom..
john.chaddock@camr.org.uk

SOURCE: Infection and immunity, (2000 May) 68 (5) 2587-93.
Journal code: 0246127. ISSN: 0019-9567.
COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 20000622
Last Updated on STN: 20000622
Entered Medline: 20000613

ABSTRACT:
Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types by a mechanism that involves cleavage of specific components of the vesicle docking/fusion complex, the SNARE complex. A derivative of the type A neurotoxin from Clostridium botulinum (termed LH(N)/A) that retains catalytic activity can be prepared by proteolysis. The LH(N)/A, however, lacks the putative native binding domain (H(C)) of the neurotoxin and is thus unable to bind to neurons and effect inhibition of neurotransmitter release. Here we report the chemical conjugation of LH(N)/A to an alternative cell-binding ligand, wheat germ agglutinin (WGA). When applied to a variety of cell lines, including those that are ordinarily resistant to the effects of neurotoxin, WGA-LH(N)/A conjugate potently inhibits secretory responses in these cells. Inhibition of release is demonstrated to be ligand mediated and dose dependent and to occur via a mechanism involving endopeptidase-dependent cleavage of the natural botulinum neurotoxin type A substrate. These data confirm that the function of the H(C) domain of C. botulinum neurotoxin type A is limited to binding to cell surface moieties. The data also demonstrate that the endopeptidase and translocation functions of the neurotoxin are effective in a range of cell types, including those of nonneuronal origin. These observations lead to the conclusion that a clostridial endopeptidase conjugate that can be used to investigate SNARE-mediated processes in a variety of cells has been successfully generated.

CONTROLLED TERM: Animals
*Botulinum Toxin Type A: ME, metabolism
Cell Line
*Clostridium botulinum: ME, metabolism
*Endopeptidases: ME, metabolism
Glycine: ME, metabolism
Insulin: ME, metabolism
*Neurons: ME, metabolism
Neurotransmitters: ME, metabolism
PC12 Cells
Rats
Tritium

Wheat Germ Agglutinins: IP, isolation & purification

AS REGISTRY NO.: Wheat Germ Agglutinins: ME, metabolism
10028-17-8 (Tritium); 11061-68-0 (Insulin); 56-40-6 (Glycine)

CHEMICAL NAME: 0 (Botulinum Toxin Type A); 0 (Neurotransmitters); 0 (Wheat Germ Agglutinins); EC 3.4.- (Endopeptidases)

82 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2000.706999 CAPLUS

DOCUMENT NUMBER: 133:261538

TITLE: Use of a lectin or lectin conjugate for modulation of C-fiber activity, and therapeutic use thereof

INVENTOR(S): Foster, Keith Alan; Chaddock, John

APPL.

INVENTOR: Andrew; Quinn, Conrad Padraig
PATENT ASSIGNEE(S): Microbiological Research Authority, UK
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000057897	A1	20001005	WO 2000-GB1247	20000331
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1165114	A1	20020102	EP 2000-914295	20000331
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
PRIORITY APPLN. INFO.:			GB 1999-7429	A 19990331
			WO 2000-GB1247	W 20000331

D Entered STN: 06 Oct 2000
B The invention relates to the treatment of pain and to compds. that modulate C-fiber activity. In particular, the invention relates to the use of a lectin in the manuf. of a medicament for modulation of C-fiber neuron activity, and to lectin conjugates. The lectin conjugates comprise a lectin coupled to a peptide or protein, wherein the peptide or protein is substantially free of Clostridial neurotoxin enzyme activity. The invention also concerns methods for manufg. the conjugates. The compds. and compns. described have particular application in the treatment of diseases of which C-fiber activity is a component. Such diseases include pain, inflammation, psoriasis and other C-fiber related conditions.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

APP.

=> fil capl; d que l15; d que l19; d que l22

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FILE COVERS 1907 - 3 Jun 2004 VOL 140 ISS 23

FILE LAST UPDATED: 2 Jun 2004 (20040602/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

'OBI' IS DEFAULT SEARCH FIELD FOR 'CAPLUS' FILE

L10 705 SEA FILE=CAPLUS ABB=ON NERVE/CT(L) (C/OBI(W) (FIBER#/OBI OR FIBRE#/OBI))

L11 900 SEA FILE=CAPLUS ABB=ON ERYTHRINA/OBI

L12 24970 SEA FILE=CAPLUS ABB=ON LECTIN#/OBI

L14 487 SEA FILE=CAPLUS ABB=ON ECL/OBI OR ECA/OBI

L15 1 SEA FILE=CAPLUS ABB=ON L10 AND (L14 OR (L11 AND L12))

L11 900 SEA FILE=CAPLUS ABB=ON ERYTHRINA/OBI

L12 24970 SEA FILE=CAPLUS ABB=ON LECTIN#/OBI

L16 97353 SEA FILE=CAPLUS ABB=ON NEURON#/OBI

L17 143736 SEA FILE=CAPLUS ABB=ON NERVE/CT

L19 3 SEA FILE=CAPLUS ABB=ON ((L16 OR L17)) AND ((L11 AND L12))

L10 705 SEA FILE=CAPLUS ABB=ON NERVE/CT(L) (C/OBI(W) (FIBER#/OBI OR FIBRE#/OBI))

L12 24970 SEA FILE=CAPLUS ABB=ON LECTIN#/OBI

L22 6 SEA FILE=CAPLUS ABB=ON L10 AND L12 AND (MUCUS/OBI OR PAIN/OBI)

=> s (l15 or l19 or l22) not l6

L83 7 (L15 OR L19 OR L22) NOT (L6)

=> fil medl; d que l38; d que l39

FILE 'MEDLINE' ENTERED AT 12:58:07 ON 03 JUN 2004

FILE LAST UPDATED: 2 JUN 2004 (20040602/UP). FILE COVERS 1951 TO DATE.

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for details. OLDMEDLINE now back to 1951.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2004 vocabulary. See <http://www.nlm.nih.gov/mesh/> and http://www.nlm.nih.gov/pubs/techbull/nd03/nd03_mesh.html for a description of changes.

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
L29      152 SEA FILE=MEDLINE ABB=ON  ERYTHRINA/CT
L30      71561 SEA FILE=MEDLINE ABB=ON  NERVE FIBERS+NT/CT
L38      0 SEA FILE=MEDLINE ABB=ON  L29 AND L30

L7       1861 SEA FILE=MEDLINE ABB=ON  C FIBER#
L28      61554 SEA FILE=MEDLINE ABB=ON  LECTINS+NT/CT
L29      152 SEA FILE=MEDLINE ABB=ON  ERYTHRINA/CT
L30      71561 SEA FILE=MEDLINE ABB=ON  NERVE FIBERS+NT/CT
L31      956 SEA FILE=MEDLINE ABB=ON  L7 AND L30
L36      5223 SEA FILE=MEDLINE ABB=ON  PLANT LECTINS/CT
L39      2 SEA FILE=MEDLINE ABB=ON  (L36 OR (L28 AND L29)) AND L31
```

=> s l39 not l34

L84 2 L39 NOT (L34)

=> fil embase;d que l51

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FILE COVERS 1974 TO 28 May 2004 (20040528/ED)

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```
L44      330 SEA FILE=EMBASE ABB=ON  ERYTHRINA
L46      1169 SEA FILE=EMBASE ABB=ON  NERVE FIBER C/CT
L51      0 SEA FILE=EMBASE ABB=ON  L44 AND L46
```

=> fil napra;d que l60

FILE 'NAPRALERT' ENTERED AT 12:58:09 ON 03 JUN 2004
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L55 397 SEA FILE=NAPRALERT ABB=ON ERYTHRINA
L56 929 SEA FILE=NAPRALERT ABB=ON NEURON? OR NERVE#
L60 0 SEA FILE=NAPRALERT ABB=ON L55.(S)L56

=> fil CANCERLIT, DRUGU, PASCAL, JICST-EPLUS, BIOTECHNO, ESBIODASE, CABA, LIFESCI, BIOSIS, TOXCENTER, WPIDS, SCISEARCH

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=> d que 172; d que 175

L66 4582 SEA ERYTHRINA OR CRISTAGALLI OR CRISTA GALLI
L67 134434 SEA LECTIN#
L70 2355985 SEA NEURON? OR NERVE?
L72 33 SEA L66 AND L67 AND L70

L66 4582 SEA ERYTHRINA OR CRISTAGALLI OR CRISTA GALLI
 L70 2355985 SEA NEURON? OR NERVE?
 L71 45291 SEA C(5A) (FIBER# OR FIBRE#)
 L75 2 SEA L66 AND L70 AND L71

=> s 172 or 175

L85 33 L72 OR L75

=> fil uspatf; d que 181

FILE 'USPATFULL' ENTERED AT 12:58:19 ON 03 JUN 2004
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FILE COVERS 1971 TO PATENT PUBLICATION DATE: 3 Jun 2004 (20040603/PD)
 FILE LAST UPDATED: 3 Jun 2004 (20040603/ED)
 HIGHEST GRANTED PATENT NUMBER: US6745393
 HIGHEST APPLICATION PUBLICATION NUMBER: US2004107471
 CA INDEXING IS CURRENT THROUGH 3 Jun 2004 (20040603/UPCA)
 ISSUE CLASS FIELDS (/INCL) CURRENT THROUGH: 3 Jun 2004 (20040603/PD)
 REVISED CLASS FIELDS (/NCL) LAST RELOADED: Apr 2004
 USPTO MANUAL OF CLASSIFICATIONS THESAURUS ISSUE DATE: Apr 2004

>>> USPAT2 is now available. USPATFULL contains full text of the <<<
 >>> original, i.e., the earliest published granted patents or <<<
 >>> applications. USPAT2 contains full text of the latest US <<<
 >>> publications, starting in 2001, for the inventions covered in <<<
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 >>> records and may be searched in standard search fields, e.g., /PN, <<<
 >>> /PK, etc. <<<

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 >>> enter this cluster. <<<
 >>> <<<
 >>> Use USPATAL when searching terms such as patent assignees, <<<
 >>> classifications, or claims, that may potentially change from <<<
 >>> the earliest to the latest publication. <<<

This file contains CAS Registry Numbers for easy and accurate
 substance identification.

L78 12209 SEA FILE=USPATFULL ABB=ON (NERVE# OR NEURON?)/IT, TI, AB, CLM
 L81 1 SEA FILE=USPATFULL ABB=ON ERYTHRINA AND L78

=> dup rem 184,183,185,181

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FILE 'PASCAL' ENTERED AT 12:58:56 ON 03 JUN 2004

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PROCESSING COMPLETED FOR L84

PROCESSING COMPLETED FOR L83

PROCESSING COMPLETED FOR L85

PROCESSING COMPLETED FOR L81

L86 26 DUP REM L84 L83 L85 L81 (17 DUPLICATES REMOVED)

ANSWERS '1-2' FROM FILE MEDLINE

ANSWERS '3-9' FROM FILE CAPLUS

ANSWERS '10-12' FROM FILE DRUGU

ANSWERS '13-14' FROM FILE PASCAL

ANSWER '15' FROM FILE ESBIOBASE

ANSWERS '16-21' FROM FILE BIOSIS

ANSWER '22' FROM FILE TOXCENTER

ANSWER '23' FROM FILE WPIDS

ANSWERS '24-25' FROM FILE SCISEARCH

ANSWER '26' FROM FILE USPATFULL

=> d iall 1-25; d ibib ab hit 26; fil hom

L86 ANSWER 1 OF 26 MEDLINE on STN

ACCESSION NUMBER: 2001130385 MEDLINE

DOCUMENT NUMBER: PubMed ID: 11113318

TITLE: Localization of N-methyl-D-aspartate NR2B subunits on
primary sensory neurons that give rise to small-caliber
sciatic nerve fibers in rats.

AUTHOR: Ma Q P; Hargreaves R J

CORPORATE SOURCE: Department of Pharmacology, Merck Sharp & Dohme Research
Laboratories, Neuroscience Research Centre, Terlings Park,
CM20 2QR, Harlow, UK.. qingping_ma@merck.com

SOURCE: Neuroscience, (2000) 101 (3) 699-707.
Journal code: 7605074. ISSN: 0306-4522.

PUB. COUNTRY: United States
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
 LANGUAGE: English
 FILE SEGMENT: Priority Journals
 ENTRY MONTH: 200103
 ENTRY DATE: Entered STN: 20010404
 Last Updated on STN: 20010404
 Entered Medline: 20010301

ABSTRACT:

In the present study we have used immunohistochemical staining and retrograde tracing techniques to investigate the relationship between the N-methyl-D-aspartate receptor NR2B subunits and small-diameter primary afferent dorsal root ganglion neurons that give rise to the sciatic nerve fibers. Three days after an intra-sciatic nerve injection of tetramethyl rhodamine isothiocyanate-conjugated wheat germ agglutinin which labels small-diameter primary afferents, many NR2B and wheat germ agglutinin-double-labeled cells (approximately 70% of wheat germ agglutinin-labeled neurons) were observed in the L5 dorsal root ganglia. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated Bandeiraea simplicifolia agglutinin isolectin B4 which labels predominantly non-peptidergic C-fiber primary afferents, NR2B and Bandeiraea simplicifolia agglutinin isolectin B4 double-labeled neurons (approximately 90% of Bandeiraea simplicifolia agglutinin isolectin B4-labeled neurons) were also observed in the L5 dorsal root ganglion. Three days after an intra-sciatic nerve injection of fluorescein isothiocyanate-conjugated cholera toxin B subunit, only approximately 40% of cholera toxin B subunit-labeled neurons were NR2B positive and those labeled neurons tended to be small-sized. When calcitonin gene-related peptide and NR2B were labeled by a double immunofluorescent staining technique, we found that the majority of calcitonin gene-related peptide-positive neurons was NR2B immunoreactive (>90% of calcitonin gene-related peptide-positive neurons, and approximately 60% of NR2B-positive neurons) as well. Size frequency analysis also demonstrated that NR2B subunits were predominantly localized on the small and medium-sized neurons. These results suggest that NR2B subunits are predominantly expressed on small diameter primary afferents, and these NR2B containing N-methyl-D-aspartate receptors may play a role in the modulation of neurotransmitter release from primary afferent terminals.

CONTROLLED TERM: Animals
 Calcitonin Gene-Related Peptide: ME, metabolism
 Cell Count
 Cell Size: PH, physiology
 Cholera Toxin: PD, pharmacology
 Fluorescein-5-isothiocyanate: DU, diagnostic use
 Lectins: DU, diagnostic use
 *Nerve Fibers: ME, metabolism
 Nerve Fibers: UL, ultrastructure
 *Neurons, Afferent: ME, metabolism
 Neurons, Afferent: UL, ultrastructure
 Nociceptors: ME, metabolism
 Nociceptors: UL, ultrastructure
 *Pain: ME, metabolism
 *Plant Lectins
 Rats
 Rats, Sprague-Dawley
 *Receptors, N-Methyl-D-Aspartate: ME, metabolism
 *Sciatic Nerve: ME, metabolism
 Sciatic Nerve: UL, ultrastructure
 Wheat Germ Agglutinins: DU, diagnostic use
 CAS REGISTRY NO.: 3326-32-7 (Fluorescein-5-isothiocyanate); 83652-28-2 (Calcitonin Gene-Related Peptide); 9012-63-9 (Cholera Toxin)
 CHEMICAL NAME: 0 (Griffonia simplicifolia lectins); 0 (Lectins); 0 (NR2B)

NMDA receptor); 0 (Plant Lectins); 0 (Receptors,
N-Methyl-D-Aspartate); 0 (Wheat Germ Agglutinins)

L86 ANSWER 2 OF 26 MEDLINE on STN
ACCESSION NUMBER: 94110395 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8282849
TITLE: Structure, vascularization, and innervation of the
mystacial pad of the rat as revealed by the lectin
Griffonia simplicifolia.
AUTHOR: Rice F L
CORPORATE SOURCE: Department of Anatomy, Cell Biology and Neurobiology,
Albany Medical College, New York 12208.
SOURCE: Journal of comparative neurology, (1993 Nov 15) 337 (3)
386-99.
Journal code: 0406041. ISSN: 0021-9967.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199402
ENTRY DATE: Entered STN: 19940228
Last Updated on STN: 19940228
Entered Medline: 19940217

ABSTRACT:

The mystacial pad of the rat is endowed with rows of vibrissal follicle-sinus complexes (F-SCs) that receive a dense and rich variety of innervation, much of which is C fibers. Each F-SC consists of a follicle at the core of a spindle-shaped, encapsulated vascular sinus. Previous studies have shown that the B subunit of the lectin Griffonia simplicifolia (GSA I-B4) binds selectively to a subset of small neurons in the trigeminal ganglion and to a subset of C fibers preferentially distributed to inner lamina II and outer lamina III of nucleus caudalis in the brainstem trigeminal complex in the rat. These laminae are also a major site of termination for afferents in superficial vibrissal nerves (SVNs) that innervate the upper portion of F-SCs. To determine the peripheral distribution of the afferents that bind GSA I-B4, mystacial pads from rats were prepared for fluorescence microscopy with GSA I-B4 conjugated to rhodamine. At the neck of each F-SC, numerous circumferentially oriented bundles of fine-caliber axonal profiles were labeled in the inner conical body, which receives nearly all of its innervation from the SVNs. A sparse, random distribution of fine-caliber profiles from deep vibrissal nerves was labeled at the level of the cavernous sinus in the deep half of the F-SCs. GSA I-B4 also labeled a variety of nonneural structures. By binding to vascular linings, GSA I-B4 revealed a dense, highly organized capillary system within the mesenchymal sheath that forms the inner lining of the vascular sinuses. Thus each F-SC appears to have a closed capillary system within the open vascular sinus. Trabeculae within the lumen of the cavernous sinus were also revealed to span between the sinus capsule and the mesenchymal sheath only about midway along the length of the follicle instead of the entire deeper half, as was previously believed. In addition, GSA I-B4 bound to the surface of follicular cells preferentially in the superficial half of the F-SCs. Sweat glands within the intervibrissal fur and some cells within sebaceous glands in F-SCs were also labeled as well as their ducts. The potential functional implications of these various features are discussed.

CONTROLLED TERM: Check Tags: Male; Support, Non-U.S. Gov't
Animals
Axons: ME, metabolism
Histocytochemistry
Lectins
Microcirculation: PH, physiology
Neurons, Afferent: PH, physiology
*Plant Lectins

Presynaptic Terminals: ME, metabolism

Rats

Rats, Sprague-Dawley

Sebaceous Glands: CY, cytology

Sebaceous Glands: IR, innervation

Sweat Glands: CY, cytology

Sweat Glands: IR, innervation

Trigeminal Ganglion: CY, cytology

*Vibrissae: AH, anatomy & histology

CHEMICAL NAME: 0 (Griffonia simplicifolia lectins); 0 (Lectins); 0 (Plant Lectins)

L86 ANSWER 3 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3

ACCESSION NUMBER: 1999:249106 CAPLUS

DOCUMENT NUMBER: 130:276767

ENTRY DATE: Entered STN: 23 Apr 1999

TITLE: Conjugates of galactose-binding lectins and clostridial neurotoxins as analgesics

INVENTOR(S): Duggan, Michael John; Chaddock, John Andrew

PATENT ASSIGNEE(S): The Speywood Laboratory Limited, UK; Microbiological Research Authority

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

INT. PATENT CLASSIF.:

MAIN:

A61K047-48

CLASSIFICATION: 1-11 (Pharmacology)

Section cross-reference(s): 63

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

3/3/99 10/7/98

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9917806	A1	19990415	WO 1998-GB3001	19981007
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306350	AA	19990415	CA 1998-2306350	19981007
AU 9893574	A1	19990427	AU 1998-93574	19981007
AU 741456	B2	20011129		
ZA 9809138	A	19990527	ZA 1998-9138	19981007
EP 996468	A1	20000503	EP 1998-946571	19981007
EP 996468	B1	20030521		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
JP 2001518522	T2	20011016	JP 2000-514674	19981007
AT 240747	E	20030615	AT 1998-946571	19981007
PT 996468	T	20030930	PT 1998-946571	19981007
PRIORITY APPLN. INFO.:			GB 1997-21189	A 19971008
			WO 1998-GB3001	W 19981007

ABSTRACT:

A class of novel agents that are able to modify nociceptive afferent function is provided. The agents may inhibit the release of neurotransmitters from discrete populations of neurons and thereby reduce or preferably prevent the transmission of afferent pain signals from peripheral to central pain fibers. They comprise a galactose-binding lectin linked to a deriv. of a clostridial

neurotoxin. The deriv. of the clostridial neurotoxin comprises the L-chain, or fragment thereof, which includes the active proteolytic enzyme domain of the light (L) chain, linked to a mol. or domain with membrane-translocating activity. The agents may be used in or as pharmaceuticals for the treatment of pain, particularly chronic pain.

UPPL. TERM: analgesic neurotoxin conjugate galactose binding
lectin

NDEX TERM: Analgesics
Molecular cloning
(conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Agglutinins and **Lectins**
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(galactose-binding, conjugates with clostridial neurotoxins; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Bandeiraea simplicifolia
Erythrina
Erythrina corallodendron
Erythrina crista-galli
Peanut (Arachis hypogaea)
Pseudomonas aeruginosa
Soybean (Glycine max)
(**lectins** of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: **Nerve**
(motor, binding to; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Neurohormones
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(neuromodulators, release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Transport proteins
ROLE: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence)
(neurotoxin domain contg.; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Clostridium
Clostridium botulinum
Clostridium tetani
(neurotoxin of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

NDEX TERM: Toxins
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(neurotoxins, of Clostridium; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: Neurotransmitters
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: Nerve
(sensory, nociceptive; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: Oligosaccharides, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (.alpha.- and .beta.-D-galactosyl; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 1811-31-0, N-Acetylgalactosamine
ROLE: BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 107231-12-9, Botulin
ROLE: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses) (conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 59-23-4, Galactose, biological studies
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (**lectins** binding; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 9001-92-7, Proteinase
ROLE: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence) (neurotoxin domain contg.; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

DEX TERM: 56-40-6, Glycine, biological studies 56-86-0, Glutamic acid, biological studies 33507-63-0, Substance p
ROLE: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process) (release of; conjugates of galactose-binding **lectins** and clostridial neurotoxins as analgesics)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD.

REFERENCE(S): (1) Allergan Inc; WO 9428923 A 1994 CAPLUS
(2) Dolly, J; WO 9532738 A 1995 CAPLUS
(3) Foster, K; WO 9633273 A 1996 CAPLUS
(4) Foster, K; WO 9807864 A 1998 CAPLUS
(5) Pascual, D; WO 9718790 A 1997 CAPLUS
(6) Streit; J Histochem Cytochem 1985, V33(10), P1042 CAPLUS

6 ANSWER 4 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 9
SESSION NUMBER: 1988:184082 CAPLUS
CUMENT NUMBER: 108:184082
TRY DATE: Entered STN: 28 May 1988
TLE: Occurrence and distribution of glycoconjugates in human tissues as detected by the **Erythrina**

cris tagalli **lectin**
 THOR(S): Vierbuchen, Mathias; Uhlenbruck, Gerhard; Ortmann, Monika; Dufhues, Gabriele; Fischer, Robert
 RPORATE SOURCE: Inst. Pathol., Univ. Cologne, Cologne, D-5000, Fed. Rep. Ger.
 URCE: Journal of Histochemistry and Cytochemistry (1988), 36(4), 367-76
 CODEN: JHCYAS; ISSN: 0022-1554
 CUMENT TYPE: Journal
 NGUAGE: English
 ASSIFICATION: 13-1 (Mammalian Biochemistry)
 Section cross-reference(s): 9

STRACT:
 rseradish peroxidase-E. cris tagalli agglutinin (HRP-ECA) conjugate was used
 or histochem. staining of tissue sections from various formalin-fixed,
 raffin-embedded human tissue specimens. The HRP-ECA conjugate showed broad
 activity, but there was a distinct distribution of native (not masked by
 alic acid) and sialic acid-masked ECA binding sites in the various organs.
 ree ECA binding sites could be detected on red blood cells; lymphocytes of the
 ymus, tonsil, and lymph node; and in mucous substances of different organs.
 ependent of blood group type, the vascular endothelium exhibited strong ECA
 activity. Free ECA binding sites occurred in the cytoplasm of Kupffer's
 ells in liver; in histiocytic cells of thymus, lymph node, and tonsil; and in
 one marrow. Podocytes of kidney glomerulus, syncytiotrophoblasts of placenta,
 egakaryocytes in bone marrow, myelin sheath of nerve, medullary thymocytes,
 d hepatocytes, as well as pancreatic islet cells, contained only sialic
 id-capped ECA binding sites. Inhibition studies with galactose, lactose, and
 acetyllactosamine, as well as other sugars, revealed that this lectin is
 ecific for galactosyl residues. ON comparison to galactose and lactose,
 acetyllactosamine exhibited the highest inhibitory activity on lectin
 nding, supporting the concept that this lectin is most reactive with
 acetyllactosamine-type (type 2 chain)glycoconjugates.

UPPL. TERM: acetyllactosamine glycoconjugate organ distribution;
Erythrina lectin glycoconjugate organ
 staining

INDEX TERM: Organ
 (acetyllactosamine-contg. glycoconjugates distribution
 in, of human)

INDEX TERM: Sialic acids
 ROLE: BIOL (Biological study)
 (acetyllactosamine-contg. glycoconjugates masking by, in
 human tissues)

INDEX TERM: Lymphocyte
 (acetyllactosamine-contg. glycoconjugates of, in human
 tissues)

INDEX TERM: Adrenal cortex, composition
 Blood vessel, composition
 Bone marrow, composition
 Bronchi
 Digestive tract
 Epididymis
 Erythrocyte
 Histiocyte
 Kidney, composition
 Lymph gland
 Mammary gland
 Muscle, composition
Nerve, composition
 Ovary, composition
 Oviduct
 Pancreas, composition

Placenta
Prostate gland
Stomach, composition
Testis, composition
Thymus gland
Thyroid gland, composition
Tonsil
Uterus, composition
(acetyllactosamine-contg. glycoconjugates of, of human)
INDEX TERM: **Erythrina** crista-galli
(**lectin** of, glycoconjugates of human organs
staining by and specificity of)
INDEX TERM: Agglutinins and **Lectins**
ROLE: BIOL (Biological study)
(of **Erythrina** cristagalli, acetyllactosamine
glycoconjugates staining by, in human organs)
INDEX TERM: Megakaryocyte
Pancreatic islet of Langerhans
(sialic acid-capped acetyllactosamine-contg.
glycoconjugates of, of human)
INDEX TERM: Staining, biological
(with **lectin** of **Erythrina**
cristagalli, in human organs)
INDEX TERM: Liver, composition
(Kupffer cell, acetyllactosamine-contg. glycoconjugates
of, of human)
INDEX TERM: Bladder
(epithelium, acetyllactosamine-contg. glycoconjugates of,
of human)
INDEX TERM: Ureter
(epithelium, acetyllactosamine-contg. glycoconjugates, of
human)
INDEX TERM: Reproductive tract
(female, acetyllactosamine-contg. glycoconjugates of, of
human)
INDEX TERM: Liver, composition
(hepatocyte, sialic acid-capped acetyllactosamine-contg.
glycoconjugates of, of human)
INDEX TERM: Reproductive tract
(male, acetyllactosamine-contg. glycoconjugates of, of
human)
INDEX TERM: Salivary gland
(submandibular, acetyllactosamine-contg. glycoconjugates
of, of human)
INDEX TERM: Trophoblast
(syncytio-, sialic acid-capped acetyllactosamine-contg.
glycoconjugates of, of human)
INDEX TERM: Thymus gland
(thymocyte, sialic acid-capped acetyllactosamine-contg.
glycoconjugates of, of human)
INDEX TERM: 59-23-4, D-Galactose, biological studies 63-42-3, Lactose
ROLE: BIOL (Biological study)
(**lectin** of **Erythrina** cristagalli
specificity for)
INDEX TERM: 32181-59-2D, N-Acetyllactosamine, glycoconjugates contg.
ROLE: BOC (Biological occurrence); BSU (Biological study,
unclassified); BIOL (Biological study); OCCU (Occurrence)
(of organs, of human, occurrence and distribution of)

86 ANSWER 5 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2004:312287 CAPLUS
DOCUMENT NUMBER: 140:315072

ENTRY DATE: Entered STN: 16 Apr 2004
TITLE: Methods and compounds for the treatment of
mucus hypersecretion by inhibiting
mucus secretion using compounds having
targeting and translocating modified light chain of
clostridial neurotoxin
INVENTOR(S): Quinn, Conrad Padraig; Foster, Keith Alan; Chaddock,
John
PATENT ASSIGNEE(S): Health Protection Agency, USA
SOURCE: U.S. Pat. Appl. Publ., 19 pp., Cont.-in-part of U.S.
6,632,440.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K039-08
US PATENT CLASSIF.: 424239100; 514012000
CLASSIFICATION: 1-9 (Pharmacology)
Section cross-reference(s): 63
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004071736	A1	20040415	US 2003-633698	20030805
WO 2000010598	A2	20000302	WO 1999-GB2806	19990825
WO 2000010598	A3	20000615		
W: AU, CA, JP, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 6632440	B1	20031014	US 2001-763669	20010529

PRIORITY APPLN. INFO.: GB 1998-18548 A 19980825
WO 1999-GB2806 W 19990825
US 2001-763669 A2 20010529

ABSTRACT:
A method of treating mucus hypersecretion, the causative factor in chronic obstructive pulmonary disease (COPD), asthma and other clin. conditions involving COPD, comprises administering a compd. that inhibits exocytosis in mucus secreting cells or neurons that control or direct mucus secretion. Also described is a compd., for use in the treatment of hypersecretion of mucus, which inhibits mucus secretion by inhibiting mucus secretion by mucus secreting cells, and/or inhibiting neurotransmitter release from neuronal cells controlling or directing mucus secretion. The compd. comprises: (a) a light chain (L-chain) or L-chain fragment of a clostridial neurotoxin, which L-chain or L-chain fragment includes the active proteolytic enzyme domain of the L-chain; (b) a targeting domain that binds to a target cell selected from the group consisting of (i) a mucus secreting cell, and (ii) a neuronal cell controlling or directing mucus secretion; and (c) a translocating domain that translocates the L-chain or L-chain fragment into the target cell; with the proviso that the compd. is not a botulinum toxin. Substance P, as the targeting domain, was conjugated to clostridial neurotoxin fragment LHN/A.

SUPPL. TERM: **mucus** hypersecretion treatment clostridial
neurotoxin light chain construct; targeting translocating
clostridial neurotoxin proteolytic construct; chronic
obstructive pulmonary disease treatment; antiasthmatic
mucus secretion inhibitor; substance P conjugate
clostridial neurotoxin light chain

INDEX TERM: Nerve
(C-fiber, targeting cells of;
treatment of **mucus** hypersecretion by inhibiting
mucus secretion using compds. having targeting

and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Lung
(Clara cell, targeting; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(F, translocating domain of, of SER virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Glycoproteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, translocating domain of, of vesicular stomatitis virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(aerosols; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Lung, disease
(chronic obstructive, treatment of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(construct contg. translocating domain of bacterial; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Eubacteria
Microorganism
Virus
(construct contg. translocating domain of protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(diphtheria, translocating domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (exotoxin A, translocating domain of domain II of pseudomonas; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (fusogenic, translocating domain of, of Semliki Forest virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Neurotransmitters
ROLE: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study) (inhibition of release of, by neurons controlling **mucus** secretion; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Exocytosis
Secretion (process) (inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Biological transport
(intracellular, construct with domain for; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Fusion proteins (chimeric proteins)
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (membrane, translocating domain of virally-expressed; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (microbial, construct contg. translocating domain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(nasal; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Nerve

(neuron, controlling **mucus** secretion, inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Nerve
(nonadrenergic-noncholinergic, targeting cells of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Clostridium botulinum
(not toxin of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Drug delivery systems
(oral; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Animal cell
(secreting **mucus**, inhibition of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Gland
(submucosal, targeting **mucus**-secreting cells of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Protein motifs
(targeting and translocating domains; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Epithelium
(targeting goblet cell of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Cell
(targeting serous; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: Toxins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tetanus, construct contg. light chain of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

INDEX TERM: SER virus
(translocating domain of F protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and

translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Pseudomonas
(translocating domain of domain II of exotoxin A of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Spumavirus
(translocating domain of envelope glycoprotein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Envelope proteins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(translocating domain of foamy virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Semliki Forest virus
(translocating domain of fusogenic protein of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Vesicular stomatitis virus
(translocating domain of glycoprotein G of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Influenza virus
(translocating domain of hemagglutinin of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Hemagglutinins
ROLE: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(translocating domain of influenza virus; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Antiasthmatics
Drug delivery systems
Human
Mucus
(treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified light chain of clostridial neurotoxin)

NDEX TERM: Asthma
(treatment of; treatment of **mucus** hypersecretion by inhibiting **mucus** secretion using compds. having targeting and translocating modified

light chain of clostridial neurotoxin)
INDEX TERM: Agglutinins and Lectins
ROLE: BSU (Biological study, unclassified); PAC
(Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(wheat germ, conjugates with LHN/A; treatment of
mucus hypersecretion by inhibiting **mucus**
secretion using compds. having targeting and
translocating modified light chain of clostridial
neurotoxin)
INDEX TERM: Adrenoceptor agonists
(.beta.2-, targeting domain of; treatment of
mucus hypersecretion by inhibiting **mucus**
secretion using compds. having targeting and
translocating modified light chain of clostridial
neurotoxin)
INDEX TERM: 9001-92-7, Proteolytic enzyme
ROLE: BSU (Biological study, unclassified); PAC
(Pharmacological activity); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(protease, domain of clostridial neurotoxin light chain;
treatment of **mucus** hypersecretion by inhibiting
mucus secretion using compds. having targeting
and translocating modified light chain of clostridial
neurotoxin)
INDEX TERM: 33507-63-0, Substance P (peptide) 37221-79-7, Vasoactive
intestinal polypeptide 80043-53-4, Gastrin-releasing
peptide 83652-28-2, Calcitonin gene-related peptide
ROLE: BSU (Biological study, unclassified); PAC
(Pharmacological activity); PRP (Properties); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
(targeting domain of; treatment of **mucus**
hypersecretion by inhibiting **mucus** secretion
using compds. having targeting and translocating modified
light chain of clostridial neurotoxin)
INDEX TERM: 33507-63-0DP, Substance P (peptide), conjugates with LHN/A
ROLE: BSU (Biological study, unclassified); PAC
(Pharmacological activity); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
(treatment of **mucus** hypersecretion by
inhibiting **mucus** secretion using compds. having
targeting and translocating modified light chain of
clostridial neurotoxin)
INDEX TERM: 679058-76-5
ROLE: PRP (Properties)
(unclaimed protein sequence; methods and compds. for the
treatment of **mucus** hypersecretion by inhibiting
mucus secretion using compds. having targeting
and translocating modified light chain of clostridial
neurotoxin)
INDEX TERM: 54017-28-6 91859-00-6 117138-19-9 158734-08-8
259653-92-4 259653-93-5 302566-59-2
ROLE: PRP (Properties)
(unclaimed sequence; methods and compds. for the
treatment of **mucus** hypersecretion by inhibiting
mucus secretion using compds. having targeting
and translocating modified light chain of clostridial
neurotoxin)

ACCESSION NUMBER: 2003:991382 CAPLUS
DOCUMENT NUMBER: 140:31455
ENTRY DATE: Entered STN: 21 Dec 2003
TITLE: Therapeutic conjugate consisting of a MEK inhibitor
and a targeting agent
INVENTOR(S): Lee, Kevin; Ho, Michael Ting Bong
PATENT ASSIGNEE(S): Cambridge Biotechnology Ltd., UK
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
INT. PATENT CLASSIF.:
MAIN: A61K047-48
SECONDARY: A61K047-46
CLASSIFICATION: 63-5 (Pharmaceuticals)
Section cross-reference(s): 14, 15
FAMILY ACC. NUM. COUNT: 1
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PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003103717	A1	20031218	WO 2003-GB2501	20030611
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG			

PRIORITY APPLN. INFO.: GB 2002-13383 A 20020611

ABSTRACT:

Conjugates for use in the treatment of pain, particularly chronic pain are described. The conjugates comprise a MEK inhibitor and a targeting agent. The targeting agent targets the MEK inhibitor to sensory neurons, thereby reducing the dosage of MEK inhibitor required to treat chronic pain. Methods of treating chronic pain using the conjugates are also described.

SUPPL. TERM: analgesic MEK mitogen activated protein kinase inhibitor
chronic **pain**
INDEX TERM: Nerve
(A.delta.-fibers; conjugate consisting of a MEK inhibitor
and a targeting agent for chronic **pain**)
INDEX TERM: Biological transport
(axonal, facilitators; conjugate consisting of a MEK
inhibitor and a targeting agent for chronic **pain**
)
INDEX TERM: Nerve
(c-fibers; conjugate consisting of a
MEK inhibitor and a targeting agent for chronic
pain)
INDEX TERM: Drug delivery systems
(carriers; conjugate consisting of a MEK inhibitor and a
targeting agent for chronic **pain**)
INDEX TERM: Pain
(chronic; conjugate consisting of a MEK inhibitor and a
targeting agent for chronic **pain**)
INDEX TERM: Analgesics
Arthritis

Neoplasm

(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Agglutinins and **Lectins**

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Spinal cord

(dorsal horn; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Receptors

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(**lectin**, IB4; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Antibodies

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(monoclonal; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Nerve, disease

(neuropathy, **pain** from; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Inflammation

(**pain** from; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Nerve

(sensory, drug targeting to; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Drug delivery systems

(targeted; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

Nerve growth factor receptors

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(targeting of; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

9061-61-4, Nerve growth factor 109511-58-2D, u0126, conjugates 167869-21-8D, Pd98059, conjugates

ROLE: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

INDEX TERM:

142805-58-1, MEK

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(inhibitors; conjugate consisting of a MEK inhibitor and a targeting agent for chronic **pain**)

REFERENCE COUNT:

13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L86 ANSWER 7 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:828902 CAPLUS

DOCUMENT NUMBER: 140:87993

ENTRY DATE: Entered STN: 22 Oct 2003

TITLE: Distribution of antinociceptive adenosine A1 receptors in the spinal cord dorsal horn, and relationship to primary afferents and neuronal subpopulations

AUTHOR(S): Schulte, G.; Robertson, B.; Fredholm, B. B.; DeLander, G. E.; Shortland, P.; Molander, C.

CORPORATE SOURCE: Department of Neuroscience, Karolinska Institutet, Stockholm, SE-171 77, Swed.

SOURCE: Neuroscience (Oxford, United Kingdom) (2003), 121(4), 907-916

CODEN: NRSCDN; ISSN: 0306-4522

PUBLISHER: Elsevier Science Ltd.

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 2-8 (Mammalian Hormones)

ABSTRACT: Adenosine can reduce pain and allodynia in animals and man, probably via spinal adenosine A1 receptors. In the present study, the authors investigate the distribution of the adenosine A1 receptor in the rat spinal cord dorsal horn using immunohistochem., in situ hybridization, radioligand binding, and confocal microscopy. In the lumbar cord dorsal horn, dense immunoreactivity was seen in the inner part of lamina II. This was unaltered by dorsal root section or thoracic cord hemisection. Confocal microscopy of the dorsal horn revealed close anatomical relationships but no or only minor overlap between A1 receptors and immunoreactivity for markers assocd. with primary afferent central endings: calcitonin gene-related peptide, or isolectin B4, or with neuronal subpopulations: .mu.-opioid receptor, neuronal nitric oxide synthase, met-enkephalin, parvalbumin, or protein kinase C.gamma., or with glial cells: glial fibrillary acidic protein. A few adenosine A1 receptor pos. structures were double-labeled with .alpha.-amino-3-hydroxy-5-methyl-4-isoaxolepropionic acid glutamate receptor subunits 1 and 2/3. The results indicate that most of the adenosine A1 receptors in the dorsal horn are located in inner lamina II postsynaptic neuronal cell bodies and processes whose functional and neurochem. identity is so far unknown. Many adenosine A1 receptor pos. structures are in close contact with isolectin B4 pos. C-fiber primary afferents and/or postsynaptic structures contg. components of importance for the modulation of nociceptive information.

SUPPL. TERM: adenosine A1 receptor pain sensory neuron dorsal horn rat

INDEX TERM: Glutamate receptors

ROLE: BSU (Biological study, unclassified); BIOL (Biological study)

(AMPA-binding; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

INDEX TERM: Adenosine receptors

ROLE: BSU (Biological study, unclassified); BIOL (Biological

study)
(A1; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Nerve**
(C-fiber; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Nerve**
(GABAergic; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Glutamate receptors**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR1 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Glutamate receptors**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR2 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Glutamate receptors**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(GluR3 subunit; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Nerve**
(cell body; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Analgesia**
Astrocyte
Pain
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Glial fibrillary acidic protein**
Parvalbumins
Synaptophysin
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Spinal cord**
(dorsal horn; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

NDEX TERM: **Agglutinins and Lectins**
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(isolectins, B4; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and

relationship to primary afferents and neuronal subpopulations)

INDEX TERM: Nerve
(neuron, excitatory- and inhibitory-; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

INDEX TERM: Nerve
(primary sensory; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

INDEX TERM: Opioid receptors
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(.mu.-opioid; distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

INDEX TERM: 58569-55-4, Met-enkephalin 83652-28-2, Calcitonin gene-related peptide 141436-78-4, Protein kinase C.gamma. 506430-87-1, Neuronal nitric oxide synthase
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(distribution of antinociceptive adenosine A1 receptors in rat spinal cord dorsal horn and relationship to primary afferents and neuronal subpopulations)

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD.

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L86 ANSWER 8 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:128418 CAPLUS

DOCUMENT NUMBER: 139:255171

ENTRY DATE: Entered STN: 20 Feb 2003

TITLE: Differential response properties of IB4-positive and
-negative unmyelinated sensory neurons to protons and
capsaicin

AUTHOR(S): Dirajlal, Sahera; Pauers, Laura E.; Stucky, Cheryl L.
CORPORATE SOURCE: Department of Cell Biology, Neurobiology and Anatomy,
Medical College of Wisconsin, Milwaukee, WI,
53226-0509, USA

SOURCE: Journal of Neurophysiology (2003), 89(1), 513-524
CODEN: JONEA4; ISSN: 0022-3077

PUBLISHER: American Physiological Society

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 1-11 (Pharmacology)

Section cross-reference(s): 13, 14

ABSTRACT:

Activation of unmyelinated (C-fiber) nociceptors by noxious chems. plays a
crit. role in the initiation and maintenance of injury-induced pain. C-fiber
nociceptors can be divided into two groups in which one class depends on nerve
growth factor during postnatal development and contains neuropeptides, and the
second class depends on glial cell line-derived neurotrophic factor during

postnatal development and contains few neuropeptides but binds isolectin B4 (IB4). We detd. the sensitivity of these two populations to protons and capsaicin using whole cell recordings of dorsal root ganglion neurons from adult mouse. IB4-neg. unmyelinated neurons were significantly more responsive to protons than IB4-pos. neurons in a concn.-dependent manner. Approx. 86% of IB4-neg. neurons responded to pH 5.0 with an inward current compared with only 33% of IB4-pos. neurons. The subtypes of proton-evoked currents in IB4 neg. unmyelinated neurons were also more diverse. Many IB4 neg. neurons exhibited transient, rapidly inactivating proton currents as well as sustained proton currents. In contrast, IB4 pos. neurons never displayed transient proton currents and responded to protons only with sustained, slowly inactivating inward currents. The two classes of neurons also responded differently to capsaicin. Twice as many naive IB4-neg. unmyelinated neurons responded to 1 μ M capsaicin as IB4-pos. neurons, and the capsaicin-evoked currents in IB4 neg. neurons were approx. 4-fold larger than those in IB4 pos. neurons. Interestingly, proton exposure altered the capsaicin responsiveness of the two classes of neurons in opposite ways. Brief pre-exposure to protons increased the no. of capsaicin-responsive IB4-pos. neurons by 2-fold and increased the capsaicin-evoked currents by 3-fold. Conversely, proton exposure decreased the no. of capsaicin-responsive IB4-neg. neurons by 50%. These data suggest that IB4 neg. unmyelinated nociceptors are initially the primary responders to both protons and capsaicin, but IB4-pos. nociceptors have a unique capacity to be sensitized by protons to capsaicin-receptor agonists.

SUPPL. TERM: isolectin B4 receptor unmyelinated sensory neuron proton
capsaicin antinociceptive; analgesic capsaicin proton C
fiber nociceptor isolectin B4 receptor

INDEX TERM: **Nerve**
 (C-fiber; differential response
 properties of isolectin B4-pos. and -neg. unmyelinated
 sensory neurons to protons and capsaicin)

INDEX TERM: Electric potential
 (biol., action; differential response properties of
 isolectin B4-pos. and -neg. unmyelinated sensory neurons
 to protons and capsaicin)

INDEX TERM: Analgesics
 Pain
 (differential response properties of isolectin B4-pos.
 and -neg. unmyelinated sensory neurons to protons and
 capsaicin)

INDEX TERM: **Pain receptors**
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (differential response properties of isolectin B4-pos.
 and -neg. unmyelinated sensory neurons to protons and
 capsaicin)

INDEX TERM: Receptors
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (lectin, for isolectin B4; differential
 response properties of isolectin B4-pos. and -neg.
 unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: Sodium channel
 ROLE: BSU (Biological study, unclassified); BIOL (Biological
 study)
 (role; differential response properties of isolectin
 B4-pos. and -neg. unmyelinated sensory neurons to protons
 and capsaicin)

INDEX TERM: Biological transport
 (uptake, of protons; differential response properties of
 isolectin B4-pos. and -neg. unmyelinated sensory neurons
 to protons and capsaicin)

INDEX TERM: 12408-02-5, Hydrogen ion, biological studies
ROLE: BSU (Biological study, unclassified); BIOL (Biological study)
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

INDEX TERM: 404-86-4, Capsaicin
ROLE: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential response properties of isolectin B4-pos. and -neg. unmyelinated sensory neurons to protons and capsaicin)

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L86 ANSWER 9 OF 26 CAPLUS COPYRIGHT 2004 ACS on STN

ACCESSION NUMBER: 2003:41375 CAPLUS

DOCUMENT NUMBER: 138:215729

ENTRY DATE: Entered STN: 17 Jan 2003

TITLE: GFR .alpha.2/neurturin signalling regulates noxious heat transduction in isolectin B4-binding mouse sensory neurons

AUTHOR(S): Stucky, Cheryl L.; Rossi, Jari; Airaksinen, Matti S.; Lewin, Gary R.

CORPORATE SOURCE: Growth Factors and Regeneration Group, Department of Neuroscience, Max Delbruck Center for Molecular Medicine, Berlin, D-13092, Germany

SOURCE: Journal of Physiology (Cambridge, United Kingdom) (2002), 545(1), 43-50

CODEN: JPHYA7; ISSN: 0022-3751

PUBLISHER: Cambridge University Press

DOCUMENT TYPE: Journal

LANGUAGE: English

CLASSIFICATION: 2-10 (Mammalian Hormones)

ABSTRACT:

The GFR .alpha.2 receptor is the cognate co-receptor for the neurotrophic factor neurturin and GFR .alpha.2 is selectively expressed by isolectin B4 (IB4)-binding nociceptive sensory neurons. Here, the authors used two physiol. approaches in combination with mice that have a targeted deletion of the GFR .alpha.2 gene (GFR .alpha.2 -/- mice) to det. whether GFR .alpha.2/neurturin signaling regulates the functional properties or the survival of IB4-binding nociceptors. Because 50% of IB4-binding neurons respond to noxious heat and because patch clamp recordings of isolated dorsal root ganglion sensory neurons allow one to neurochem. identify subpopulations of neurons, the authors analyzed the noxious heat responsiveness of IB4-pos. and -neg. small-diam. neurons isolated from adult GFR .alpha.2 -/- and littermate control mice. The percentage of IB4-pos. neurons that had large (> 100 pA) heat-evoked inward currents was severely reduced in GFR .alpha.2 -/- mice (12%) compared to wild-type littermates (47%), and this loss in large-magnitude heat currents was accounted for by an increase in neurons with very small (< 100 pA) heat-evoked currents as well as an increase in neurons with no detectable heat current. Counts of IB4-pos. and -neg. neurons, as well as counts of unmyelinated axons in the saphenous nerve, confirmed that the loss in neurons with large-amplitude heat currents was due to a deficit in heat transduction and not a decrease in cell survival. The effect was modality specific for heat because mech. transduction of all fiber types, including IB4-pos. C fibers, was normal. The authors' data are the first to indicate a transduction-function role for GFR

alpha.2/neurturin signaling in a specific class of sensory neurons.

UPPL. TERM: neurotrophic factor receptor GFR alpha heat signaling
isolectin B4; **pain** receptor skin signaling
isolectin B4 sensory neuron mouse

NDEX TERM: **Nerve**
(C-fiber; GFR .alpha.2/neurturin
signaling regulates noxious heat transduction in
isolectin B4-binding mouse sensory neurons)

NDEX TERM: **Pain**
Signal transduction, biological
(GFR .alpha.2/neurturin signaling regulates noxious heat
transduction in isolectin B4-binding mouse sensory
neurons)

NDEX TERM: **Pain receptors**
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(GFR .alpha.2/neurturin signaling regulates noxious heat
transduction in isolectin B4-binding mouse sensory
neurons)

NDEX TERM: **Neurotrophic factor receptors**
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(GFR-.alpha.2; GFR .alpha.2/neurturin signaling regulates
noxious heat transduction in isolectin B4-binding mouse
sensory neurons)

NDEX TERM: **Axon**
(diam.; GFR .alpha.2/neurturin signaling regulates
noxious heat transduction in isolectin B4-binding mouse
sensory neurons)

NDEX TERM: **Temperature effects, biological**
(heat, noxious; GFR .alpha.2/neurturin signaling
regulates noxious heat transduction in isolectin
B4-binding mouse sensory neurons)

NDEX TERM: **Agglutinins and Lectins**
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(isolectins, B4; GFR .alpha.2/neurturin signaling
regulates noxious heat transduction in isolectin
B4-binding mouse sensory neurons)

NDEX TERM: **Nerve**
(myelinated; GFR .alpha.2/neurturin signaling regulates
noxious heat transduction in isolectin B4-binding mouse
sensory neurons)

NDEX TERM: **Skin**
(sensory neuron; GFR .alpha.2/neurturin signaling
regulates noxious heat transduction in isolectin
B4-binding mouse sensory neurons)

NDEX TERM: **Nerve**
(sensory, skin; GFR .alpha.2/neurturin signaling
regulates noxious heat transduction in isolectin
B4-binding mouse sensory neurons)

NDEX TERM: 185857-51-6, Neurturin
ROLE: BSU (Biological study, unclassified); BIOL (Biological
study)
(GFR .alpha.2/neurturin signaling regulates noxious heat
transduction in isolectin B4-binding mouse sensory
neurons)

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CAPLUS

L86 ANSWER 10 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN DUPLICATE 2
 ACCESSION NUMBER: 2003-12380 DRUGU P
 TITLE: Inhibition of release of neurotransmitters from rat dorsal
 root ganglia by a novel conjugate of a Clostridium botulinum
 toxin A endopeptidase fragment and **Erythrina**
cristagalli lectin.
 AUTHOR: Duggan M J; Quinn C P; Chaddock J A; Purkiss J R; Alexander F
 C G; Doward S J F; Fooks S J; Friis L M; Hall Y H J; Kirby E
 R
 CORPORATE SOURCE: Centre-App.Micro+Res.Porton-Down; Univ.London
 LOCATION: Salisbury; London, U.K.
 SOURCE: J.Biol.Chem. (277, No. 38, 34846-52, 2002) 4 Fig. 34 Ref.
 CODEN: JBCHA3 ISSN: 0021-9258
 AVAIL. OF DOC.: Center for Applied Microbiology and Research, Porton Down,
 Salisbury, Wiltshire SP4 0JG, England. (J.A.C., 18 authors).
 (e-mail: john.chaddock@camr.org.uk).
 LANGUAGE: English
 DOCUMENT TYPE: Journal

ABSTRACT:

The catalytically active derivative (LHN) of the type A neurotoxin from
 Clostridium botulinum was coupled to a **lectin** obtained from
 Erythrina **cristagalli** (ECL, Sigma-Chem.) to form a novel

conjugate. Chemical conjugates prepared between ECL and either native (n) or recombinant (r) LHN inhibited substance P release from embryonic dorsal root ganglia (eDRG) and glycine from embryonic spinal cord **neuron** (eSCN). The dependence of inhibition of neurotransmitter release on the cleavage of SNAP-25 was shown through the use of an endopeptidase-deficient LHN conjugate variant. The duration of action of inhibition of neurotransmitter released by the LHN-ECL in-vitro was similar to that seen with C. botulinum neurotoxin (BT). These findings suggest that the inhibition of release of neurotransmitters from a **neuronal** population of therapeutic relevance to the treatment of pain can be achieved.

SECTION HEADING: P Pharmacology

CLASSIF. CODE: 60 Autonomic

CONTROLLED TERM:

NEURON *FT; **GANGLION** *FT; **TISSUE-CULTURE** *FT;
IN-VITRO *FT; **SNAP-25** *FT; **COUPLING** *FT; **GLYCINE** *FT;
AMINOACID-METAB. *FT; **MOUSE** *FT; **IN-VIVO** *FT; **CLEAVAGE** *FT;
CONJUGATE *FT; **INTRATHECAL** *FT; **I.P.** *FT; **LAB.ANIMAL** *FT;
INJECTION *FT

[01] **SIGMA-CHEM.** *FT; **LECTIN** *FT; **ERYTHRINA**

*FT; **CRYSTAGALLI** *FT; **PH** *FT

[02] **BOTULINUM-A-TOXIN** *PH; **BOTULATOX** *RN; **NATIVE** *FT; **RECOMBINANT**

*FT; **SPASMOLYTICS** *FT; **TOXINS** *FT; **PH** *FT

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L86 ANSWER 11 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-27692 DRUGU A S

TITLE: Characterisation of a novel conjugate of a botulinum neurotoxin A endopeptidase fragment and E. **cristagalli lectin**.

AUTHOR: Ling R J; Fretwell R; Alexander F; Fooks S; Leeds N; Jameson K; Hall Y; Kirby E; Chaddock J; Stone C

LOCATION: Salisbury, U.K.

SOURCE: Arch.Pharmacol. (365, Suppl. 2, R28, 2002) 1 Ref.

CODEN: NSAPCC ISSN: 0028-1298

AVAIL. OF DOC.: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 OJG, England.

LANGUAGE: English

DOCUMENT TYPE: Journal

ABSTRACT:

The aim of this study was to prepare novel molecules with a selectivity for nociceptive **neurons**. Using the 2-domain LHN fragment of BoNT/A or recombinant recLHN/A, conjugates were prepared with a Coral Tree **lectin** (**Erythrina cristagalli**: ECL). A much improved toxicity profile in mice was demonstrated for the conjugates compared to the whole toxin. In-vitro in **neuronal** cultures in-vitro, the equivalency of the recLHN/A-ECL and the nLHN/A-ECL conjugates were demonstrated. These data represent an important step forward in the pursuit of establishing the therapeutic potential of retargeted endopeptidases. (conference abstract: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins, Hannover, Germany, 2002).

SECTION HEADING: A Analysis
S Adverse Effects

CLASSIF. CODE: 34 Toxicology
59 CNS and Motor

65 Drug Delivery
70 Analysis

CONTROLLED TERM:

[01] IN-VITRO *FT; TOX. *FT; CONJUGATE *FT; LECTIN *FT;
IN-VIVO *FT; MOUSE *FT; TARGETING *FT; NEURON *FT;
LAB.ANIMAL *FT; DRUG-DELIVERY *FT; OC *FT; AE *FT

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L86 ANSWER 12 OF 26 DRUGU COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2002-27671 DRUGU P S

TITLE: Retargeted clostridial endopeptidase: antinociceptive activity in preclinical models of pain.

AUTHOR: Cui M; Chaddock J A; Rubino J; Khanijou S; Duggan M J; Walsh B; Foster K A; Aoki K R

CORPORATE SOURCE: Allergan

LOCATION: Irvine, Cal., USA; Salisbury, U.K.

SOURCE: Arch.Pharmacol. (365, Suppl. 2, R16, 2002)

CODEN: NSAPCC ISSN: 0028-1298

AVAIL. OF DOC.: Allergan Inc., 2525 Dupont Drive, Irvine, CA92612, U.S.A.

LANGUAGE: English

DOCUMENT TYPE: Journal

ABSTRACT:

A fragment of botulinum neurotoxin A lacking the binding domain (LHn/A) was chemically conjugated to **Erythrina cristagalli** ***lectin*** (ECL) to produce LHn/A-ECL. This conjugate was tested following i.t. and s.c. administration in the murine hot plate model, rat formalin model and Chung model (all models of acute pain). The results showed that LHn/A-ECL is a novel agent designed to selectively deliver the endopeptidase activity of botulinum neurotoxin to nociceptive afferent **neurons**. It displayed long-lasting analgesic properties in a range of in-vivo models of pain. LHn/A-ECL did not produce any muscle weakness. (conference abstract: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins, Hannover, Germany, 2002).

SECTION HEADING: P Pharmacology
S Adverse Effects

CLASSIF. CODE: 34 Toxicology
43 Analgesics, NSAIDs
65 Drug Delivery

CONTROLLED TERM:

[01] PAIN *OC; INTRATHECAL *FT; S.C. *FT; IN-VIVO *FT; RAT *FT;
MOUSE *FT; ANALGESIC *FT; CONJUGATE *FT; DRUG-DELIVERY *FT;
SIDE-EFFECT-ABSENT *FT; ANIMAL-MODEL *FT; LAB.ANIMAL *FT; PH
*FT; AE *FT

FIELD AVAIL.: AB; LA; CT

FILE SEGMENT: Literature

L86 ANSWER 13 OF 26 PASCAL COPYRIGHT 2004 INIST-CNRS. ALL RIGHTS RESERVED.
on STN DUPLICATE 1

ACCESSION NUMBER: 2004-0228708 PASCAL

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TITLE (IN ENGLISH): Retargeted clostridial endopeptidases: Inhibition of nociceptive neurotransmitter release in vitro, and antinociceptive activity in in vivo models of pain
Basic and Therapeutic Aspects of Neurotoxins

AUTHOR: CHADDOCK John A.; PURKISS John R.; ALEXANDER Frances C. G.; DOWARD Sarah; FOOKS Sarah J.; FRIIS Lorna M.; HALL Yper H. J.; KIRBY Elizabeth R.; LEEDS Nicola; MOULSDALE Hilary J.; DICKENSON Anthony; GREEN G. Mark; RAHMAN Wahida; SUZUKI Rie; DUGGAN Michael J.; QUINN Conrad P.; SHONE Clifford C.; FOSTER Keith A. BIGALKE HANS (ed.); DRESSLER Dirk (ed.); JANKOVIC Joseph (ed.)

CORPORATE SOURCE: Health Protection Agency, Porton Down, Salisbury, Wiltshire, United Kingdom; University College London, University College, Gower Street, London, United Kingdom
Institute of Toxicology, Medical School of Hannover, Hannover, Germany, Federal Republic of; Department of Neurology, Rostock University, Rostock, Germany, Federal Republic of; Parkinson's Disease Center and Movement Disorders Clinic, Department of Neurology, Baylor College of Medicine, Houston, Texas, United States

SOURCE: Movement disorders, (2004), 19(SUP8), 42-47, 22 refs. Conference: Toxins 2002. Conference, Hannover (Germany, Federal Republic of), 2002
ISSN: 0885-3185

DOCUMENT TYPE: Journal; Conference

BIBLIOGRAPHIC LEVEL: Analytic

COUNTRY: United States

LANGUAGE: English

AVAILABILITY: INIST-20953, 354000113591720060

ABSTRACT: Clostridial neurotoxins potently and specifically inhibit neurotransmitter release in defined cell types. Previously reported data have demonstrated that the catalytically active LH.sub.N endopeptidase fragment of botulinum neurotoxin type A (termed LH.sub.N/A) can be retargeted to a range of cell types in vitro to lead to inhibition of secretion of a range of transmitters. Here, we report the synthesis of endopeptidase conjugates with in vitro selectivity for nociceptive afferents compared to spinal neurons. Chemical conjugates prepared between **Erythrina cristagalli lectin** and LH.sub.N/A are assessed in vitro and in in vivo models of pain. Chemical conjugates prepared between **E. cristagalli lectin** and either natively sourced LH.sub.N/A. or recombinant LH.sub.N/A purified from Escherichia coli are assessed, and equivalence of the recombinant material is demonstrated. The duration of action of inhibition of neurotransmitter release by the conjugate in vitro is also assessed and is comparable to that observed with Clostridium botulinum neurotoxin. Selectivity of targeting and therapeutic potential have been confirmed by in vivo electrophysiology studies. Furthermore, the analgesic properties of the conjugate have been assessed in in vivo models of pain and extended duration effects observed. These data provide proof of principle for the concept of retargeted clostridial endopeptidases as novel analgesics.

CLASSIFICATION CODE: 002B17; Life sciences; Medical sciences; Neurology, Nervous system

CONTROLLED TERM: Nervous system diseases; Endopeptidase; Neuromediator; Neurotransmitter; Biological activity; Pain

READER TERM: Peptidases; Hydrolases; Enzyme

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on STN DUPLICATE 7

ACCESSION NUMBER: 1995-0359246 PASCAL
COPYRIGHT NOTICE: Copyright .COPYRG. 1995 INIST-CNRS. All rights reserved.

TITLE (IN ENGLISH): **Lectin** and immunohistochemical comparison of glycoconjugates in the conjunctiva of patients with and without exfoliation syndrome

AUTHOR: HIETANEN J.; UUSITALO M.; TARKKANEN A.; KIVELAE T.
CORPORATE SOURCE: Helsinki univ. cent. hosp., dep. ophthalmology, 00290 Helsinki, Finland

SOURCE: British journal of ophthalmology, (1995), 79(5), 467-472, 33 refs.
ISSN: 0007-1161 CODEN: BJOPAL

DOCUMENT TYPE: Journal
BIBLIOGRAPHIC LEVEL: Analytic
COUNTRY: United Kingdom
LANGUAGE: English
AVAILABILITY: INIST-1015, 354000050929870160
ABSTRACT: Aims-The study was carried out to search for labelling similar to that of intraocular exfoliation material in the conjunctiva by light microscopy using **lectin** and immunohistochemistry. Methods-Ten formalin fixed and paraffin embedded conjunctival biopsy specimens both from patients with and without exfoliation syndrome were studied with a panel of 11 **lectins** and with three monoclonal antibodies to the HNK-1 carbohydrate epitope, all of which react with intraocular exfoliation material. Results-The **lectin** binding profile was essentially the same in specimens from patients with and without exfoliation syndrome. The superficial epithelium reacted similarly with Phaseolus vulgaris (PHA-E), Caragana arborescens (CAA), Helix pomatia (HPA), concanavalin A (ConA), and wheat germ (WGA) agglutinins. Binding was also detected with peanut (PNA) and Bauhinia purpurea (BPA) agglutinins, particularly in patients with exfoliation. The basement membrane generally reacted with Ricinus communis (RCA-I), PHA-E, Vicia villosa (VVA), ConA, and Lens culinaris (LCA) agglutinins. The stroma was weakly labelled with RCA-I, PHA-E, ConA, and LCA. **Lectin** binding to the vascular endothelium was moderate with RCA-I, PHA-E, CAA, ConA, LCA, and WGA. Inconsistent labelling was also detected with PNA, BPA, and **Erythrina cristagalli** agglutinin (ECA). The subendothelial region reacted weakly but consistently with PHA-E, ConA, and LCA, and inconsistently with PNA. Pretreatment with neuraminidase did not change that pattern. Antibodies to the HNA-I epitope reacted only with myelinated stromal **nerve** branches. Conclusion-No evidence of abnormal deposits in any specimen was found. The carbohydrate composition of intraocular exfoliation material may differ from that of exfoliation-like fibres often detected in the conjunctiva by electron microscopy

CLASSIFICATION CODE: 002B09G; Life sciences; Medical sciences; Ophthalmology

CONTROLLED TERM: Exfoliation; Lens; Immunohistochemistry; **Lectin**; Glycoconjugate; Conjunctiva; Optical

BROADER TERM: microscopy; Exploration; Human
Eye disease; Lens disease; Pathology

L86 ANSWER 15 OF 26 Elsevier BIOBASE COPYRIGHT 2004 Elsevier Science B.V.
on STN DUPLICATE

ACCESSION NUMBER: 1998221674 ESBIODASE

TITLE: **Lectin** binding patterns in the vomeronasal organ and accessory olfactory bulb of the rat

AUTHOR: Salazar I.; Sanchez Quinteiro P.

CORPORATE SOURCE: I. Salazar, Departamento Anatomia y Embriologia, Facultad de Veterinaria de Lugo, Universidad Santiago de Compostela, E-27002 Lugo, Spain.
E-mail: anigsabe@lugo usc.es

SOURCE: Anatomy and Embryology, (1998), 198/4 (331-339), 55 reference(s)
CODEN: ANEMDG ISSN: 0340-2061

DOCUMENT TYPE: Journal; Article

COUNTRY: Germany, Federal Republic of

LANGUAGE: English

SUMMARY LANGUAGE: English

ABSTRACT: A number of previous studies have indicated that **lectin** histochemistry is an obvious choice for characterizing the vomeronasal system. However, apparently inconsistent results have been obtained: notably, the affinity with which various **lectins** bind to the accessory olfactory bulb varies among taxa, even considering closely related species. In the present study, the binding patterns of seven **lectins** in the rat accessory olfactory bulb, vomeronasal **nerves** and vomeronasal duct were investigated. The *Bandeiraea simplicifolia* **lectin** bound exclusively to the vomeronasal **nerve** and glomerular layers of the accessory olfactory bulb, while the *Ulex europeus* and *Lycopersicon esculentum* **lectins** bound to these regions and additionally to the **nerve** and glomerular layers of the main olfactory bulb. Soybean agglutinin showed a similar pattern to that obtained with the *Ulex europeus* and *Lycopersicon esculentum* **lectins**, though it also faintly labelled other parts of the structures examined. The *Vicia villosa* and *Erythrina cristagalli* **lectins** were not specific for the vomeronasal system, since they labelled grey and white matters in structures including the lateral olfactory tract and the anterior olfactory nuclei. The *Dolichos biflorus* **lectin** did not bind to vomeronasal tissues. The observed patterns of binding in the accessory olfactory bulb were consistent with those observed in the vomeronasal **nerves**, but unlike those observed in the epithelium of the vomeronasal duct. This latter result probably reflects binding of **lectins** to sugar residues contained in secreted mucus rather than those in epithelial **nerve** endings.

CLASSIFICATION CODE: 88.4.14 NEUROSCIENCE: PHYSIOLOGY OF THE CENTRAL NERVOUS SYSTEM: Olfactory Bulb

SUPPLEMENTARY TERM: Accessory olfactory bulb; Vomeronasal epithelium; Vomeronasal **nerves**; Glycoproteins; Rat

L86 ANSWER 16 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 4

ACCESSION NUMBER: 2000:374003 BIOSIS
DOCUMENT NUMBER: PREV200000374003
TITLE: Role of neurotrophins and **lectins** in prevention
of ototoxicity.
AUTHOR(S): Gao, Wei-Qiang [Reprint author]
CORPORATE SOURCE: Department of Neuroscience, Genentech, Inc., 1 DNA Way,
South San Francisco, CA, 94080, USA
SOURCE: Henderson, Donald; Salvi, Richard J.; Quaranta, Antonio;
McFadden, Sandra L.; Burkard, Robert F. Ann. N. Y. Acad.
Sci., (1999) pp. 312-327. Annals of the New York Academy of
Sciences. print.
Publisher: New York Academy of Sciences, 2 East 63rd
Street, New York, NY, 10021, USA. Series: Annals of the New
York Academy of Sciences.
Meeting Info.: Conference on Ototoxicity: Basic Science and
Clinical Applications. Bari, Italy. June 18-20, 1999.
CODEN: ANYAA9. ISSN: 0077-8923. ISBN: 1-57331-204-5
(cloth), 1-57331-205-3 (paper).
DOCUMENT TYPE: Book
Conference; (Meeting)
Book; (Book Chapter)
Conference; (Meeting Paper)
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Aug 2000
Last Updated on STN: 8 Jan 2002
CONCEPT CODE: Biochemistry studies - General 10060
General biology - Symposia, transactions and proceedings
00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids
10064
Endocrine - Neuroendocrinology 17020
Sense organs - Physiology and biochemistry 20004
Sense organs - Pathology 20006
Nervous system - Physiology and biochemistry 20504
Toxicology - General and methods 22501
Tissue culture, apparatus, methods and media 32500
INDEX TERMS: Major Concepts
Sense Organs (Sensory Reception); Toxicology
INDEX TERMS: Parts, Structures, & Systems of Organisms
cochlea: sensory system, explant culture; hair cells:
nervous system, sensory system, degeneration; spiral
ganglion **neurons**: nervous system, degeneration
INDEX TERMS: Diseases
hearing loss: ear disease, toxicity, ototoxin-induced
Hearing Disorders (MeSH)
INDEX TERMS: Diseases
ototoxicity: ear disease, toxicity
INDEX TERMS: Chemicals & Biochemicals
Detura stramonium **lectin**; **Erythrina**
cristagalli lectin; brain derived
neurotrophic factor [BDNF]; cisplatin: ototoxin;
concanavalin A [Con A]: **lectin**, ototoxicity
protective effects; gentamicin: ototoxin; neurotrophin-3
[NT-3]; neurotrophin-4/5 [NT-4/5]; sodium salicylate:
ototoxin
INDEX TERMS: Miscellaneous Descriptors
Book Chapter; Meeting Paper
ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia

Organism Name

rat

Taxa Notes

Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 15663-27-1 (cisplatin)
11028-71-0 (concanavalin A)
11028-71-0 (Con A)
1403-66-3 (gentamicin)
130939-66-1 (neurotrophin-3)
130939-66-1 (NT-3)
54-21-7 (sodium salicylate)

L86 ANSWER 17 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
DUPLICATE 8

ACCESSION NUMBER: 1991/184067 BIOSIS

DOCUMENT NUMBER: PREV199191098816; BA91:98816

TITLE: **LECTIN** LOCALIZATION IN HUMAN NERVE BY
BIOCHEMICALLY DEFINED **LECTIN**-BINDING
GLYCOPROTEINS NEOGLYCOPROTEIN AND **LECTIN**-SPECIFIC
ANTIBODY.

AUTHOR(S): GABIUS H-J [Reprint author]; WOSGIEN B; HENDRYS M; BARDOSI
ACORPORATE SOURCE: MAX-PLANCK-INSTITUT FUR EXPERIMENTELLE MEDIZIN, ABTEILUNG
CHEMIE, HERMANN-REIN-STRASSE 3, W-3400 GOETTINGENSOURCE: Histochemistry, (1991) Vol. 95, No. 3, pp. 269-278.
CODEN: HCMYAL. ISSN: 0301-5564.

DOCUMENT TYPE: Article

FILE SEGMENT: BA

LANGUAGE: ENGLISH

ENTRY DATE: Entered STN: 19 Apr 1991

Last Updated on STN: 19 Apr 1991

ABSTRACT: Molecular recognition can be mediated by protein (**lectin**)
)-carbohydrate interaction, explaining the interest in this topic. Plant
lectins and, more recently, chemically glycosylated neoglycoproteins
principally allow to map the occurrence of components of this putative
recognition system. Labelled endogenous **lectins** and the
lectin -binding ligands can add to the panel of glycohistochemical
tools. They may be helpful to derive physiologically valid conclusions in this
field for mammalian tissues. Consequently, experiments were prompted to employ
the abundant .beta.-galactoside-specific **lectin** of human
nerves in affinity chromatography and in histochemistry to purify and
to localize its specific glycoprotein ligands. In comparison to the
.beta.-galactoside-specific plant **lectins** from *Ricinus communis* and
Erythrina **cristagalli**, notable similarities were especially
detectable in the respective profiles of the mammalian and the
Erythrina **lectin**. They appear to account for rather
indistinguishable staining patterns in fixed tissue sections. Inhibitory
controls within affinity chromatography, within solid-phase assays for each
fraction of **lectin**-binding glycoproteins and within histochemistry as
well as the demonstration of crossreactivity of the three fractions of
lectin -binding glycoproteins with the biotinylated **Erythrina**
lectin in blotting ascertained the specificity of the **lectin**
-glycoprotein interaction. In addition to monitoring the accessible cellular
ligand part by the endogenous **lectin** as probe, the comparison of
immunohistochemical and glycohistochemical detection of the **lectin** in
serial sections proved these methods for receptor analysis to be rather equally
effective. The observation that the biotinylated **lectin**-binding
glycoproteins are also appropriate ligands in glycohistochemical analysis
warrants emphasis. Overall, the introduction of biotinylated mammalian
lectins as well as the **lectin**-binding glycoproteins will aid
to critically evaluate the physiological significance of the glycobiological

Not
on
point

interplay between endogenous **lectins** and distinct carbohydrate parts of cellular glycoconjugates.

CONCEPT CODE: Microscopy - Histology and histochemistry 01056
Cytology - Human 02508
Biochemistry studies - Proteins, peptides and amino acids 10064
Biochemistry studies - Carbohydrates 10068
Nervous system - Physiology and biochemistry 20504
Immunology - General and methods 34502
Plant physiology - Chemical constituents 51522

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Cell Biology;
Immune System (Chemical Coordination and Homeostasis);
Methods and Techniques; Nervous System (Neural Coordination)

INDEX TERMS: Miscellaneous Descriptors
MOLECULAR RECOGNITION CELLULAR GLYCOCONJUGATE
IMMUNOHISTOCHEMISTRY

ORGANISM: Classifier
Hominidae 86215
Super Taxa
Primates; Mammalia; Vertebrata; Chordata; Animalia
Taxa Notes
Animals, Chordates, Humans, Mammals, Primates, Vertebrates

L86 ANSWER 18 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:520045 BIOSIS

DOCUMENT NUMBER: PREV200200520045

TITLE: Retargeted endopeptidase-dependent inhibition of neurotransmitters from **neurons** involved in nociception.

AUTHOR(S): Mouldsdale, H. J. [Reprint author]; Hall, Y. [Reprint author]; Kirby, E. R. [Reprint author]; Purkiss, J. R. [Reprint author]; Chaddock, J. A. [Reprint author]; Foster, K. A. [Reprint author]

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down, Salisbury, Wiltshire, SP4 0JG, UK

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June, 2002) Vol. 365, No. Supplement 2, pp. R30. print.
Meeting Info.: International Conference on Basic and Therapeutic Aspects of Botulinum and Tetanus Toxins. Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Oct 2002

Last Updated on STN: 9 Oct 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings 00520

Cytology - Animal 02506

Biochemistry studies - General 10060

Biochemistry studies - Proteins, peptides and amino acids 10064

Nervous system - Physiology and biochemistry 20504

INDEX TERMS: Major Concepts
Biochemistry and Molecular Biophysics; Nervous System (Neural Coordination)

INDEX TERMS: Parts, Structures, & Systems of Organisms
dorsal root ganglia: nervous system; **neurons**: nervous system; spinal cord: nervous system

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
; botulinum neurotoxin A; calcitonin gene related
peptide: neurotransmitter; endopeptidase; glutamate:
amino acid, neurotransmitter; substance P:
neurotransmitter

INDEX TERMS: Miscellaneous Descriptors
nociception; Meeting Abstract

REGISTRY NUMBER: 83652-28-2 (calcitonin gene related peptide)
9001-92-7 (endopeptidase)
11070-68-1 (glutamate)
33507-63-0 (substance P)

L86 ANSWER 19 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:520037 BIOSIS

DOCUMENT NUMBER: PREV200200520037

TITLE: Characterisation of a novel conjugate of a botulinum
neurotoxin A endopeptidase fragment and E.
cristagalli lectin.

AUTHOR(S): Ling, R. J. [Reprint author]; Fretwell, R.; Alexander, F.;
Fooks, S.; Leeds, N.; Jameson, K.; Hall, Y.; Kirby, E.;
Chaddock, J.; Shone, C.

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down,
Salisbury, Wiltshire, SP4 0JG, UK

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June,
2002) Vol. 365, No. Supplement 2, pp. R28. print.
Meeting Info.: International Conference on Basic and
Therapeutic Aspects of Botulinum and Tetanus Toxins.
Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Cytology - General 02502
Cytology - Animal 02506
Enzymes - General and comparative studies: coenzymes
10802
Nervous system - Physiology and biochemistry 20504

INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular
Biophysics); Nervous System (Neural Coordination)

INDEX TERMS: Parts, Structures, & Systems of Organisms
neurons: nervous system, nociceptive

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
; botulinum neurotoxin A; botulinum neurotoxin A
endopeptidase: fragment

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

L86 ANSWER 20 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:520029 BIOSIS

DOCUMENT NUMBER: PREV200200520029

TITLE: The extended duration of action of retargeted endopeptidase
in embryonic dorsal root ganglia **neurons.**

AUTHOR(S): Kirby, E. R. [Reprint author]; Mouldsdale, H. J. [Reprint
author]; Hall, Y. [Reprint author]; Chaddock, J. A.
[Reprint author]; Foster, K. A. [Reprint author]

CORPORATE SOURCE: Centre for Applied Microbiology and Research, Porton Down,
Salisbury, Wiltshire, SP4 0JG, UK

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June,
2002) Vol. 365, No. Supplement 2, pp. R26. print.
Meeting Info.: International Conference on Basic and
Therapeutic Aspects of Botulinum and Tetanus Toxins.
Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Cytology - General 02502
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids
10064
Enzymes - General and comparative studies: coenzymes
10802
Nervous system - Physiology and biochemistry 20504

INDEX TERMS: Major Concepts
Cell Biology; Enzymology (Biochemistry and Molecular
Biophysics); Nervous System (Neural Coordination)

INDEX TERMS: Parts, Structures, & Systems of Organisms
dorsal root ganglia **neurons**: nervous system,
culture, embryonic

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
[substance P]; SNAP-25; botulinum neurotoxin A;
endopeptidase

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

REGISTRY NUMBER: 9001-92-7 (endopeptidase)
33507-63-0 (SUBSTANCE P)

L86 ANSWER 21 OF 26 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:519991 BIOSIS

DOCUMENT NUMBER: PREV200200519991

TITLE: Retargeted clostridial endopeptidase: Antinociceptive
activity in preclinical models of pain.

AUTHOR(S): Cui, M. [Reprint author]; Chaddock, J. A.; Rubino, J.
[Reprint author]; Khanijou, S. [Reprint author]; Duggan, M.
J.; Walsh, B.; Foster, K. A.; Aoki, K. R. [Reprint author]

CORPORATE SOURCE: Allergan Inc., 2525 Dupont Drive, Irvine, CA, 92612, USA

SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology, (June,
2002) Vol. 365, No. Supplement 2, pp. R16. print.
Meeting Info.: International Conference on Basic and
Therapeutic Aspects of Botulinum and Tetanus Toxins.
Hannover, Germany. June 08-12, 2002.
CODEN: NSAPCC. ISSN: 0028-1298.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)

LANGUAGE: English

ENTRY DATE: Entered STN: 9 Oct 2002
Last Updated on STN: 9 Oct 2002

CONCEPT CODE: General biology - Symposia, transactions and proceedings
00520
Cytology - Animal 02506
Biochemistry studies - Proteins, peptides and amino acids
10064

Enzymes - General and comparative studies: coenzymes 10802
Pathology - Therapy 12512
Nervous system - Physiology and biochemistry 20504
Nervous system - Pathology 20506
Pharmacology - General 22002

INDEX TERMS: Major Concepts
Enzymology (Biochemistry and Molecular Biophysics);
Nervous System (Neural Coordination); Pharmaceuticals
(Pharmacology)

INDEX TERMS: Parts, Structures, & Systems of Organisms
sensory **neurons**: nervous system

INDEX TERMS: Diseases
neuropathic pain: nervous system disease
Pain (MeSH)

INDEX TERMS: Diseases
pain: nervous system disease
Pain (MeSH)

INDEX TERMS: Chemicals & Biochemicals
Erythrina cristagalli lectin
: protein; botulinum toxin A; endopeptidase

INDEX TERMS: Miscellaneous Descriptors
Meeting Abstract

ORGANISM: Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
mouse: animal model
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates,
Nonhuman Mammals, Rodents, Vertebrates

REGISTRY NUMBER: 93384-43-1 (botulinum toxin A)
9001-92-7 (endopeptidase)

L86 ANSWER 22 OF 26 TOXCENTER COPYRIGHT 2004 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 2000:104043 TOXCENTER

COPYRIGHT: Copyright 2004 ACS

DOCUMENT NUMBER: CA13213161319V

TITLE: Role of neurotrophins and **lectins** in prevention
of ototoxicity

AUTHOR(S): Gao, Wei-Qiang

CORPORATE SOURCE: Department of Neuroscience, Genentech, Inc., South San
Francisco, CA, 94080, USA.

SOURCE: Annals of the New York Academy of Sciences, (1999) Vol.
884, No. Ototoxicity, pp. 312-327.
CODEN: ANYAA9. ISSN: 0077-8923.

COUNTRY: UNITED STATES

DOCUMENT TYPE: Journal

FILE SEGMENT: CAPLUS

OTHER SOURCE: CAPLUS 2000:14944

LANGUAGE: English

ENTRY DATE: Entered STN: 20011116
Last Updated on STN: 20020409

ABSTRACT:
A review with 48 refs. Degeneration of hair cells (HC) and/or spiral ganglion
neurons (SGN) is a major cause of hearing loss. Postnatal rat cochlear
explant cultures are used to study the toxic actions of different classes of
ototoxins and to identify mols. that can protect SGN and HC from ototoxic
damage. Various ototoxins induce differential damage to HC and/or SGN. While
gentamicin preferentially causes HC death, sodium salicylate selectively
induces degeneration of SGN. In contrast, cisplatin results in destruction of

both SGN and HC. Specific neurotrophins, including NT-4/5, BDNF, and NT-3, greatly protect SGN from all three types of ototoxins. In contrast, NGF and other growth factors have no effect. Of the 51 compds. examd., only Con A, a ***lectin*** mol., significantly protects HC from gentamicin. A dose-dependent study of Con A shows that maximal protection occurred at 100 nM. Further expts. indicates that preincubation of Con A with gentamicin does not form a complex, and coaddn. of Con A and gentamicin to bacterial cultures, such as E. Coli cultures, does not interfere with the antibiotic activity of gentamicin. When the other 21 lectins are examd., **Erythrina** ***cristagalli*** lectin and Detura stramonium lectin also show activity similar to Con A. These findings may help elucidate the mechanisms of ototoxins and suggest that specific neurotrophins and ***lectins*** may be of therapeutic value in the prevention of ototoxin-induced hearing loss.

CLASSIFICATION CODE: 2-0

SUPPLEMENTARY TERMS: Miscellaneous Descriptors
review neurotrophin **lectin** hearing loss
inhibition ear

L86 ANSWER 23 OF 26 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2000-611684 [58] WPIDS
DOC. NO. CPI: C2000-183090
TITLE: Manufacturing a medicament for modulating C-fiber neurone activity and treating e.g. pain, psoriasis, inflammation or mucus hypersecretion, comprises using a **lectin** or a nucleic acid encoding a **lectin**.

DERWENT CLASS: B04 D16
INVENTOR(S): CHADDOCK, J A; FOSTER, K A; QUINN, C P
PATENT ASSIGNEE(S): (MICR-N) MICROBIOLOGICAL RES AUTHORITY
COUNTRY COUNT: 93
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG	MAIN	IPC
WO 2000057897	A1	20001005	(200058)*	EN	62	A61K038-16	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW NL OA PT SD SE SL SZ TZ UG ZW							
W: AE AG AL AM AT AU AZ BA BB BG BR BY CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW							
AU 2000035690	A	20001016	(200106)			A61K038-16	
EP 1165114	A1	20020102	(200209)	EN		A61K038-16	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI							
JP 2002540162	W	20021126	(200307)		55	A61K038-00	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2000057897	A1	WO 2000-GB1247	20000331
AU 2000035690	A	AU 2000-35690	20000331
EP 1165114	A1	EP 2000-914295	20000331
		WO 2000-GB1247	20000331
JP 2002540162	W	JP 2000-607647	20000331
		WO 2000-GB1247	20000331

FILING DETAILS:

PATENT NO	KIND	PATENT NO

 AU 2000035690 A Based on WO 2000057897
 EP 1165114 A1 Based on WO 2000057897
 JP 2002540162 W Based on WO 2000057897

PRIORITY APPLN. INFO: GB 1999-7429

19990331

INT. PATENT CLASSIF.:

MAIN: A61K038-00; A61K038-16
 SECONDARY: A61K047-48; A61K048-00; A61P001-06; A61P011-02;
 A61P011-06; A61P017-00; A61P017-06; A61P019-02;
 A61P025-00; A61P025-04; A61P025-06; A61P029-00;
 A61P043-00; C07K014-42; C07K019-00; C12N015-09;
 C12N015-29; C12P021-02

BASIC ABSTRACT:

WO 200057897 A UPAB: 20001114

NOVELTY - Manufacturing (M1) a medicament for modulation of C-
fiber neurone activity using a **lectin**.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the
 following:

(1) manufacturing (M2) a medicament for modulation of C-
fiber neurone activity using a nucleic acid that encodes
 a **lectin**;

(2) a pharmaceutical composition comprising a **lectin**, where
 the composition is free of Clostridial neurotoxin enzyme activity;

(3) a composition comprising one or more nucleic acid sequences
 encoding **lectins**;

(4) a conjugate comprising a **lectin** coupled to a peptide or
 protein that is free of Clostridial neurotoxin enzyme activity and
 optionally has a C-fiber modulation activity;

(5) a nucleic acid encoding (4);

(6) manufacturing (M3) a medicament for modulation of C-
fiber activity, using (2), (3), (4), or (5);

(7) treating pain, psoriasis, inflammation or mucus hypersecretion
 using a medicament manufactured with a **lectin** or a nucleic acid
 encoding a **lectin**;

(8) inhibiting C-fiber activity using a
 composition of (M1), (M2), or (M3);

(9) stimulating C-fiber activity using a
 composition of (M1), (M2), or (M3);

(10) modulating C-fiber activity comprising
 administering a **lectin**, (2), (3), (4) or (5) to a patient;

(11) preparing (4) comprising coupling together, optionally via a
 linker, a **lectin** and a peptide or protein; and

(12) preparing (4) comprising expressing (5) in a host, optionally
 including a linker nucleic acid sequence located within (5) to provide a
 linker molecule between the **lectin** and the peptide or protein of
 the conjugate.

ACTIVITY - Analgesic; antipsoriatic; antiinflammatory; mucolytic;
 antiasthmatic; antiulcer; antiarthritic; antiallergic; antimigraine. The
 analgesic effects of a galactosyl-reactive **lectin** IB4 from
Bandeiraea simplicifolia were studied in vivo, in adult outbred mice (MF1)
 of either sex, with a weight range of 10 - 30 g. The mice were
 anaesthetized and a 5 mm incision was made in the skin above the spinal
 column. **Lectin** IB4 was injected in a single dose into an
 intrathecal space. The incision was closed using a single wound clip and
 the mice became fully mobile within two minutes. The effect over a 10
 hour period was monitored. A significant increase in withdrawal latency
 was observed at 1 hour post application with an apparent maximal activity
 at 4 hours (15.0 and 17.6 seconds, respectively, compared to 11.6 and 12.4
 seconds for a control group injected with phosphate buffered saline
 (PBS)). Analgesia was still clearly discernable over control-group
 animals at 10 hours post application (15.7 seconds for IB4 injected

animals and 12.7 seconds for PBS-injected animals).

MECHANISM OF ACTION - Substance P release modulator; **C-fiber** activity modulator. Embryonic dorsal root ganglia (eDRG) were prepared from rats. An **Erythrina cristagalli lectin**-protein conjugate was applied to the eDRG and the substance P released was assayed. The percent inhibition of release was about 5 % at a concentration of 0.1 micro g/ml and was -45 % at 10 micro g/ml of the conjugate, demonstrating that the conjugate modulated release of substance P from an in vitro model of **C-fibers**.

USE - The new method is used for manufacturing a medicament for modulating **C-fiber neurone** activity, using a **lectin** or nucleic acid encoding a **lectin** (claimed). The medicament can be used to treat pain, psoriasis, inflammation or mucus hypersecretion (claimed). It can also be used to treat asthma, ulcer formation, headache, migraine, arthritis, and irritable bowel syndrome.

Dwg.0/14

FILE SEGMENT: CPI
FIELD AVAILABILITY: AB; DCN
MANUAL CODES: CPI: B04-E03F; B04-L01; B04-N04; B12-M01A; B12-M02;
 B14-C01; B14-C03; B14-C09; B14-E08; B14-E10C;
 B14-G02A; B14-K01A; B14-K01E; B14-N16; B14-N17C;
 D05-H17C

L86 ANSWER 24 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN
ACCESSION NUMBER: 2003:682796 SCISEARCH
THE GENUINE ARTICLE: 707JA
TITLE: Isolation of the gene and large-scale expression and purification of recombinant **Erythrina cristagalli lectin**
AUTHOR: Stancombe P R (Reprint); Alexander F C G; Ling R; Matheson M A; Shone C C; Chaddock J A
CORPORATE SOURCE: Ctr Appl Microbiol & Res, Salisbury SP4 0JG, Wilts, England (Reprint)
COUNTRY OF AUTHOR: England
SOURCE: PROTEIN EXPRESSION AND PURIFICATION, (AUG 2003) Vol. 30, No. 2, pp. 283-292.
 Publisher: ACADEMIC PRESS INC ELSEVIER SCIENCE, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495 USA.
 ISSN: 1046-5928.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 15
ABSTRACT:

Using polymerase chain reaction, the coding sequence for **Erythrina cristagalli lectin** (ECL) has been cloned and expressed in *Escherichia coli*. The amplified DNA sequence of ECL is highly homologous to that previously reported for **Erythrina corallodendron lectin** (ECorL), confirming the absence of introns in the ECL gene. The polypeptide sequences of ECL and ECorL have been compared and five amino acids have been identified that differentiate the two proteins. Recombinant E. **cristagalli lectin** (recECL) was expressed in *E. coli* from a genomic clone encoding the mature **E. cristagalli lectin** gene. Constitutive expression localised recombinant protein in inclusion bodies, which were solubilised, and recECL, subsequently refolded and purified by lactose affinity chromatography. Significant advantages were observed for purification from inclusion bodies rather than from a clone optimised to express soluble protein. A large-scale purification scheme has been developed that can prepare functional recECL from inclusion bodies with a yield of 870 mg/L culture. By the range of characterisation methods employed in this study, it has been demonstrated that recECL is functionally equivalent to native ECL obtained from the **E. cristagalli** plant. In addition, characterisation of the binding of radiolabelled recECL to cultured dorsal root ganglia

demonstrated that recECL binds to a single pool of receptors. (C) 2003 Elsevier Science (USA). All rights reserved.

CATEGORY: BIOCHEMICAL RESEARCH METHODS; BIOCHEMISTRY & MOLECULAR BIOLOGY; BIOTECHNOLOGY & APPLIED MICROBIOLOGY

SUPPLEMENTARY TERM: **Erythrina cristagalli**;
Erythrina-related **lectins**; cloning;
bacterial expression system; lactose affinity

SUPPL. TERM PLUS: DORSAL-ROOT GANGLIA; ESCHERICHIA-COLI; CORALLODENDRON
LECTIN; AGGLUTININ; PROTEINS; CLONING; SITE; RAT;
RECOGNITION; **NEURONS**

REFERENCE(S):

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
=====	=====	=====	=====	=====
ADAR R	1997	249	684	EUR J BIOCHEM
ARANGO R	1992	205	575	EUR J BIOCHEM
ARANGO R	1990	264	109	FEBS LETT
CHAO Q M	1994	313	346	ARCH BIOCHEM BIOPHYS
DUGGAN M J	2002	277	34846	J BIOL CHEM
LONGSTAFF M	1998	252	59	EUR J BIOCHEM
MORENO E	1997	36	4429	BIOCHEMISTRY-US
POLYAK S W	1997	10	615	PROTEIN ENG
SHARMA V	1996	389	289	FEBS LETT
SHARON N	1990	4	3198	FASEB J
SHARMA V	1994	148	299	GENE
SHARON N	1995	30	59	ESSAYS BIOCHEM
STREIT W J	1985	33	1042	J HISTOCHEM CYTOCHEM
SVENSSON C	2002	321	69	J MOL BIOL
WELCH M J	2000	38	245	TOXICON

L86 ANSWER 25 OF 26 SCISEARCH COPYRIGHT 2004 THOMSON ISI on STN

ACCESSION NUMBER: 92:195554 SCISEARCH

THE GENUINE ARTICLE: HK198

TITLE: BANDEIRAEA-SIMPLICIFOLIA **LECTIN**-I AND
VICIA-VILLOSA AGGLUTININ BIND SPECIFICALLY TO THE
VOMERONASAL AXONS IN THE ACCESSORY OLFACTORY-BULB OF THE
RAT

AUTHOR: ICHIKAWA M (Reprint); OSADA T; IKAI A

CORPORATE SOURCE: TOKYO METROPOLITAN INST NEUROSCI, DEPT ANAT & EMBRYOL, 2-6
MUSASHIDAI, FUCHU, FUCHU, TOKYO 183, JAPAN (Reprint);
TOKYO INST TECHNOL, FAC BIOSCI & BIOTECHNOL, DEPT BIOL
SCI, YOKOHAMA, KANAGAWA 227, JAPAN

COUNTRY OF AUTHOR: JAPAN

SOURCE: NEUROSCIENCE RESEARCH, (FEB 1992) Vol. 13, No. 1, pp.
73-79.

ISSN: 0168-0102.

DOCUMENT TYPE: Note; Journal

FILE SEGMENT: LIFE

LANGUAGE: ENGLISH

REFERENCE COUNT: 14

ABSTRACT:

The binding of 21 **lectins** to the accessory olfactory bulb (AOB) of the rat was examined by histochemistry. Two **lectins** [Bandeiraea simplicifolia **lectin** I (BSL-I) and Vicia villosa agglutinin (VVA)] bound specifically to the vomeronasal (VN) axons in the AOB. Seven **lectins***** (Datura stramonium **lectin**, **Erythrina cristagalli***** **lectin**, Lycopersicon esculentum **lectin**, Ricinus communis agglutinin I, soybean agglutinin, Solanum tuberosum **lectin*****, and Ulex europaeus agglutinin) bound to both VN axons in AOB and olfactory axons in the main olfactory bulb. BSL-I and VVA are useful as the marker of VN axons. This selective binding of **lectins** indicates

*Not
C-time*

the presence of specific glycoconjugates on the surface of VN axons.

CATEGORY: NEUROSCIENCES
 SUPPLEMENTARY TERM: **LECTIN**; GLYCOCONJUGATES; VOMERONASAL SYSTEM;
 ACCESSORY OLFACTORY BULB; RAT
 SUPPL. TERM PLUS: MEDIAL AMYGDALOID NUCLEUS; ADULT-RAT; SYNAPTIC
 REORGANIZATION; NERVOUS-SYSTEM; FIBERS; RECOVERY;
NEURONS; LESION; RABBIT
 RESEARCH FRONT: 91-0209 002; VOMERONASAL ORGAN; RAT OLFACTORY EPITHELIUM;
 MALE HAMSTERS; SEXUAL PHEROMONES

REFERENCE(S) :

Referenced Author (RAU)	Year (RPY)	VOL (RVL)	PG (RPG)	Referenced Work (RWK)
BARBER P C	1989	30	1	NEUROSCIENCE
HALPERN M	1987	10	325	ANNU REV NEUROSCI
ICHIKAWA M	1987	420	243	BRAIN RES
ICHIKAWA M	1987	420	253	BRAIN RES
ICHIKAWA M	1988	451	248	BRAIN RES
ICHIKAWA M	1989	498	45	BRAIN RES
IMAMURA K	1985	328	362	BRAIN RES
KEY B	1986	69	131	NEUROSCI LETT
MORI K	1986	365	404	BRAIN RES
MORI K	1987	408	215	BRAIN RES
MORI K	1987	20	259	NEUROSCIENCE
SCHWARTING G A	1991	547	239	BRAIN RES
STREIT W J	1985	33	1042	J HISTOCHEM CYTOCHEM
WYSOCKI C J	1979	3	301	NEUROSCIENCE BIOBEHA

L86 ANSWER 26 OF 26 USPATFULL on STN
 ACCESSION NUMBER: 2002:314377 USPATFULL
 TITLE: Endomural therapy
 INVENTOR(S): Slepian, Marvin J., Tucson, AZ, UNITED STATES
 PATENT ASSIGNEE(S): Endoluminal Therapeutics, Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2002176849	A1	20021128
APPLICATION INFO.:	US 2002-72766	A1	20020208 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-267578P	20010209 (60)
DOCUMENT TYPE:	Utility	
FILE SEGMENT:	APPLICATION	
LEGAL REPRESENTATIVE:	Patrea L. Pabst, Holland & Knight LLP, One Atlantic Center, Suite 2000, 1201 West Peachtree Street, Atlanta, GA, 30309-3400	
NUMBER OF CLAIMS:	33	
EXEMPLARY CLAIM:	1	
NUMBER OF DRAWINGS:	4 Drawing Page(s)	
LINE COUNT:	1277	

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods, devices and materials for the treatment or repair, replacement, transplantation or augmentation of tissues in endomural zones specifically by open surgical, minimally invasive or percutaneous transmural or trans parenchymal application of polymeric material alone or in combination with bioactive agents or cells, have been developed. These methods and systems are useful to repair, alter function, replace

function or augment function of the central or endomural aspects of solid organs or tubular body structures.

PI US 2002176849 A1 20021128
DETD [0082] Polymers with free carboxylic acid or other anionic groups (e.g., sulfonic acid), such as the acrylic acid polymers noted above, can be used alone or added to other polymeric formulations to enhance tissue adhesiveness. Alternatively, materials that have tissue binding properties can be added to or bound to the polymeric material. Peptides with tissue adhesion properties are discussed below. Lectins that can be covalently attached to a polymeric material to render it target specific to the mucin and mucosal cell layer could be used. Useful lectin ligands include lectins isolated from: *Abrus precatorius*, *Agaricus bisporus*, *Anguilla anguilla*, *Arachis hypogaea*, *Pandeiraea simplicifolia*, *Bauhinia purpurea*, *Caragan arobreseens*, *Cicer arietinum*, *Codium fragile*, *Datura stramonium*, *Dolichos biflorus*, **Erythrina** *corallodendron*, **Erythrina** *cristagalli*, *Euonymus europaeus*, *Glycine max*, *Helix aspersa*, *Helix pomatia*, *Lathyrus odoratus*, *Lens culinaris*, *Limulus polyphemus*, *Lysopersicon esculentum*, *Maclura pomifera*, *Momordica charantia*, *Mycoplasma gallisepticum*, *Naja mocambique*, as well as the lectins Concanavalin A, Succinyl-Concanavalin A, *Triticum vulgare*, *Ulex europaeus* I, II and III, *Sambucus nigra*, *Maackia amurensis*, *Limax fluvius*, *Homarus americanus*, *Cancer antennarius*, and *Lotus tetragonolobus*.

CLM What is claimed is:
31. The device of claim 15 for **nerve** regeneration.

IT **Nerve**
(cell or stem cell; endomural therapy)
IT 9001-92-7, Protease 9061-61-4, **Nerve** growth factor
62031-54-3, Fibroblast growth factor 62229-50-9, Epidermal growth factor 81669-70-7, Metalloprotease
(endomural therapy)

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